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(71) Applicant (for all designated States except US): **CHIRON CORPORATION** [US/US]; 4560 Horton Street, Emeryville, CA 94608-2916 (US).

(72) Inventor; and
(75) Inventor/Applicant (for US only): **RAPPUOLI, Rino** [—/US]; c/o Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US).

(74) Agent: **HALE, Rebecca, M.**; Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608-2916 (US).

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(54) Title: IMMUNOGENIC COMPOSITIONS FOR *STREPTOCOCCUS AGALACTIAE*

(57) Abstract: This application relates to Group B Streptococcus ("GBS") vaccines comprising combinations of GBS polypeptide antigens where the polypeptides contribute to the immunological response in a recipient. Preferably, the compositions of the invention comprise a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from an antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.

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IMMUNOGENIC COMPOSITIONS FOR *STREPTOCOCCUS AGALACTIAE*

This application claims the benefit and incorporates by reference in its entirety U.S. provisional application 60/548,789, filed February 26, 2004 and claims priority to International Patent Application No. PCT/US03/29167, Attorney Reference No. PP19766.002, filed on September 15, 2003, incorporated herein in its entirety.

FIELD OF THE INVENTION

The invention relates to an immunogenic antigen derived from *Streptococcus agalactiae* ("GBS") and its use in combinations with other GBS antigens to provide for broader coverage among different GBS strains. In particular, the invention relates to a composition comprising a combination of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof. The combination may include GBS 80 and at least one other GBS antigen. For example, the combination may include GBS 80 and up to thirteen GBS antigens. In a preferred embodiment, the combination may include GBS 80 and up to ten GBS antigens. In a more preferred embodiment, the combination may include GBS 80 and up to five GBS antigens. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from an antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes GBS 80 in combination with one or more of GBS 104 and GBS 322.

BACKGROUND OF THE INVENTION

GBS has emerged in the last 20 years as the major cause of neonatal sepsis and meningitis that affect 0.5 – 3 per 1000 live births, and an important cause of morbidity among the older age group affecting 5 – 8 per 100,000 of the population. Current disease management strategies rely on intrapartum antibiotics and neonatal monitoring which have reduced neonatal case mortality from >50% in the 1970's to less than 10% in the 1990's. Nevertheless, there is still considerable morbidity and mortality and the management is expensive. 15 – 35% of pregnant women are asymptomatic carriers and at high risk of transmitting the disease to their babies. Risk of neonatal infection is associated with low serotype specific maternal antibodies and high titers are believed to be protective. In addition, invasive GBS disease is increasingly recognized in elderly adults with underlying disease such as diabetes and cancer.

The "B" in "GBS" refers to the Lancefield classification, which is based on the antigenicity of a carbohydrate which is soluble in dilute acid and called the C carbohydrate. Lancefield identified 13 types of C carbohydrate, designated A to O, that could be serologically differentiated. The organisms

that most commonly infect humans are found in groups A, B, D, and G. Within group B, strains can be divided into at least 9 serotypes (Ia, Ib, Ia/c, II, III, IV, V, VI, VII and VIII) based on the structure of their polysaccharide capsule. In the past, serotypes Ia, Ib, II, and III were equally prevalent in normal vaginal carriage and early onset sepsis in newborns. Type V GBS has emerged as an important cause of GBS infection in the USA, however, and strains of types VI and VIII have become prevalent among Japanese women.

The genome sequence of a serotype V strain 2603 V/R has been published (Ref. 1) and various polypeptides for use as vaccine antigens have been identified (Ref. 2). The vaccines currently in clinical trials, however, are based on polysaccharide antigens. These suffer from serotype-specificity and poor immunogenicity, and so there is a need for effective vaccines against *S. agalactiae* infection.

It is an object of the invention to provide further and improved compositions for providing immunity against GBS disease and/or infection. The compositions are based on a combination of two or more (e.g., three or more) GBS antigens.

SUMMARY OF THE INVENTION

Applicants have discovered that an immunogenic GBS antigen, GBS 80, is particularly suitable for immunization purposes, especially when used in combination with other GBS antigens. The combination may include GBS 80 and at least one other GBS antigen or up to thirteen other GBS antigens. In a preferred embodiment, the combination may include GBS 80 and up to 10 GBS antigens. In a more preferred embodiment, the combination includes GBS 80 and up to five GBS antigens. In particular, the invention relates to a composition comprising a combination of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination consists of GBS 80, GBS 104 and GBS 322.

Instead of the full length antigen, the combination may comprise an immunogenic fragment of the selected GBS antigen and/or a polypeptide sequence having sequence identity to the selected antigen.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

DETAILED DESCRIPTION OF THE INVENTION

The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, e.g., *Remington's Pharmaceutical Sciences*, Mack Publishing Company, Easton, Pa., 19th Edition (1995); *Methods In Enzymology* (S. Colowick and N. Kaplan, eds., Academic Press, Inc.); and *Handbook of Experimental Immunology*, Vols. I-IV (D.M. Weir and C.C. Blackwell, eds., 1986, Blackwell Scientific Publications); Sambrook, et al., *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); *Handbook of Surface and Colloidal Chemistry* (Birdi, K.S. ed., CRC Press, 1997); *Short Protocols in Molecular Biology*, 4th ed. (Ausubel et al. eds., 1999, John Wiley & Sons); *Molecular Biology Techniques: An Intensive Laboratory Course*, (Ream et al., eds., 1998, Academic Press); *PCR (Introduction to Biotechniques Series)*, 2nd ed. (Newton & Graham eds., 1997, Springer Verlag); Peters and Dalrymple, *Fields Virology* (2d ed), Fields et al. (eds.), B.N. Raven Press, New York, NY.

All publications, patents and patent applications cited herein, are hereby incorporated by reference in their entireties.

GBS Antigens

As discussed above, the invention provides an immunogenic composition comprising a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof.

The combinations of GBS antigens may include polypeptide fragments of the identified GBS antigens. The length of the fragment may vary depending on the amino acid sequence of the specific GBS antigen, but the fragment is preferably at least 7 consecutive amino acids, (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200 or more). Preferably the fragment comprises one or more epitopes from the sequence. Other preferred fragments include (1) the N-terminal signal peptides of each identified GBS antigen, (2) the identified GBS antigens without their N-terminal signal peptides, and (3) each identified GBS antigen wherein up to 10 amino acid residues (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) are deleted from the N-terminus and/or the C-terminus e.g. the N-terminal amino acid residue may be deleted. Other fragments omit one or more domains of the protein (e.g. omission of a signal peptide, of a cytoplasmic domain, of a transmembrane domain, or of an extracellular domain).

The combinations of GBS antigens may include polypeptide sequences having sequence identity to the identified GBS antigens. The degree of sequence identity may vary depending on the amino acid sequence (a) in question, but is preferably greater than 50% (e.g. 60%, 65%, 70%, 75%,

80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more). Polypeptides having sequence identity include homologs, orthologs, allelic variants and functional mutants of the identified GBS antigens. Typically, 50% identity or more between two proteins is considered to be an indication of functional equivalence. Identity between proteins is preferably determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affinity gap search with parameters *gap open penalty*=12 and *gap extension penalty*=1.

The polypeptides can, of course, be prepared by various means (e.g. recombinant expression, purification from GBS, chemical synthesis *etc.*) and in various forms (e.g. native, fusions, glycosylated, non-glycosylated *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other streptococcal or host cell proteins) or substantially isolated form.

GBS 80

As discussed above, the invention relates to the use of GBS 80 in synergistic combination with other GBS antigens. GBS 80 refers to a putative cell wall surface anchor family protein.

Nucleotide and amino acid sequence of GBS 80 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8779 and SEQ ID 8780. These sequences are also set forth below as SEQ ID NOS 1 and 2:

SEQ ID NO. 1

ATGAAATATCGAAGAAGTTATTGTTTCGGCTGCTGTTTTAACAAATGGTGGCGGGGCTCAACTGTTGA
 ACCAGTAGCTCAGTTTGGCACTGGAATGAGTATTGTAAGAGCTGCGAAGGTGTCAAGAAGCGCCAG
 CGAAACACACAGTAAATATCTATAAATTACAGCTGATAGTTATAAATCGGAATTAAGTTCTAATGGT
 GGTATCGAGAATAAAGACGGCGGAAGTAATATCTAACTATGCTAACTGGTGACAAATGTAAAGGTTT
 GCAAGGTGTACAGTTTAAACGTTATAAAGTCAAGACGGGATATTTCTGTTGATGAATTGAAAAATTTGA
 CAACAGTTTGAAGCAGCAGATGCAAAAGTTGGAACGATTCTTGAAGAGGTGTCACTCTACCTCAAAA
 ACTAATGCTCAAGGTTTGGTCGTGATGCTCTGGATTCAAAAAGTAAATGTGAGATTAAGTTGATGTAGA
 AGATTTAAAGAATTCACTTCAACATTACCAAGCTTATGCTGTACCGTTTGTGTTGGAATTACCAAG
 TTGCTAACTCTACAGGTACAGGTTTCCCTTTCTGAAATTAATATTTACCCTAAAAACGTTGTAAGTAT
 GAACCAAAAACAGATAAAGATGTTAAAAAATTAGGTGAGGACGATGCAGGTATACGATTGGTGGAAGA
 ATTCAAATGGTTCTTGAATCTCAATCCCTGCCAATTTAGGTGACATGAAAAATTTGAAATTAATCTG
 ATAAATTTGCAGATGGCTTGACTTATAAATCTGTTGAAAAATCAAGATTGGTTCGAAAAACATGAAT
 AGAGATGAGCACTACACTATTGATGAACCAACAGTTGATACCAAAATACATTAATAATACGTTTTAA
 ACCAGAGAAATTTAAAGAAATTTGCTGAGCTACTTAAAGGAATGACCTTGTAAAAATCAAGATGCTC
 TTGATAAAGCTACTGCAAAATACAGATGATGCGGCATTTTGGAAATTTCCAGTTGATCACTAATTAAT
 GAAAAAGCAGTTTATAGGAAACCAATTTGAAATTAATTTTGAACCTCAATATGACCATACTCCTGATAA
 AGCTGACAAATCCAAACCATCTAATCTCCCAAGAAACAGAGTTTCACTATGGTGGGAAACGATTGG
 TAAAGAAAGACTCAACAGAAACACAAACACTAGTGGTGCTGAGTTTGATTTGTTGGTCTGATTTGG
 ACAGCAGTAAATTTGACAGATGCTCTTATTAAGCGCAATTAATAAAACATAATTGCTGGAGAGC
 TGTTACTGGGCAACCAATCAAAATTGAATCATACACAGCGGTACGTTTGGAGATTAAAGGTTTGGCTT
 ATGCAGTTGATGCGAATGACAGGGTACAGCAGTAACCTTACAAATTTAAAGAAACAAAAGCACCAGAA
 GTGTTATGTAATCCCTGATAAAGAAATCGAGTTTACAGTATCAACAACTCTTATAATACAAAACCAAC
 TGACATCAGGGTTGATAGTGCTGATGCAACACTGATACAATTTAAAAACACAAACGCTCCTTCAATCC
 CTAATACTGGTGGTATTGGTACGGCTATCTTTGTCGCTATCGGTGCTGCGGTGATGGCTTTTGCTGTT
 AAGGGGATGAAGCGTCGTACAAAAGATAAC

SEQ ID NO: 2

MKLSKKLLFSAAVLTVMAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYPKSEITSNG
 GIENKDGEVISNYAKLGDNVKGLQGVQFKRYVKVTDISVDELKKLTVEAADAKVGTILEEGVSLPQK
 TNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVT
 EPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLGDYKFEITDKFADGLTYKSVGKIKIGSKTLN
 RDEHYTIDEPTVDNQNTLKITFKPEKFKIEALLKGMTLVKNQDALDKATANTDDAAFLIIPVASTIN
 EKAVLGKAIENTFELQYDHTPPKADNPKPSNPPRKEPVHTGGKRFVKKDSSTETQTLGGAEFDLLASDG
 TAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDGTETFKGLAYAVDANAEGTAVTYKLKETKAPE
 GYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPSIPNTGGIGTAFVAIGAAMFAVFAV
 KGMKRRTKDN

As described above, the combinations of the invention may include a fragment of a GBS
 antigen. In some instances, removal of one or more domains, such as a leader or signal sequence
 region, a transmembrane region, a cytoplasmic region or a cell wall anchoring motif, may facilitate
 cloning of the gene encoding the antigen and/or recombinant expression of the GBS protein. In
 addition, fragments comprising immunogenic epitopes of the cited GBS antigens may be used in the
 compositions of the invention.

GBS 80 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO: 2 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 80 are removed. An example of such a
 GBS 80 fragment is set forth below as SEQ ID NO: 3:

SEQ ID NO: 3

AEVVSQERPAKTTVNIYKLQADSYPKSEITSNGGIENKDGEVISNYAKLGDNVKGLQGVQFKRYVKVTDI
 SVDELKKLTVEAADAKVGTILEEGVSLPQKTNQAGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYA
 VPFVLELPVANSTGTGFLSEINIYPKNVVTDEPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLGM
 DYKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFKIEALLKGM
 TLVKNQDALDKATANTDDAAFLIIPVASTINEKAVLGKAIENTFELQYDHTPPKADNPKPSNPPRKEP
 VHTGGKRFVKKDSSTETQTLGGAEFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHTDG
 TETFKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTI
 KNNKRPSIPNTGGIGTAFVAIGAAMFAVFAV KGMKRRTKDN

GBS 80 contains a C-terminal transmembrane region which is indicated by the underlined
 sequence near the end of SEQ ID NO: 2 above. In one embodiment, one or more amino acids from
 the transmembrane region and/or a cytoplasmic region are removed. An example of such a GBS 80
 fragment is set forth below as SEQ ID NO: 4:

SEQ ID NO: 4

MKLSKKLLFSAAVLTVMAGSTVEPVAQFATGMSIVRAAEVSQERPAKTTVNIYKLQADSYPKSEITSNG
 GIENKDGEVISNYAKLGDNVKGLQGVQFKRYVKVTDISVDELKKLTVEAADAKVGTILEEGVSLPQK
 TNAQGLVVDALDSKSNVRYLYVEDLKNSPSNITKAYAVPFVLELPVANSTGTGFLSEINIYPKNVVT
 EPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLGDYKFEITDKFADGLTYKSVGKIKIGSKTLN
 RDEHYTIDEPTVDNQNTLKITFKPEKFKIEALLKGMTLVKNQDALDKATANTDDAAFLIIPVASTIN
 EKAVLGKAIENTFELQYDHTPPKADNPKPSNPPRKEPVHTGGKRFVKKDSSTETQTLGGAEFDLLASDG

TAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHDTGTFEIKGLAYAVDANAEGTAVTYKLKETKAPE
GYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPS *IPNTG*

GBS 80 contains an amino acid motif indicative of a cell wall anchor: **SEQ ID NO: 5**

5 *IPNTG* (shown in *italics* in **SEQ ID NO: 2** above). In some recombinant host cell systems, it may be preferable to remove this motif to facilitate secretion of a recombinant GBS 80 protein from the host cell. Accordingly, in one preferred fragment of GBS 80 for use in the invention, the transmembrane and/or cytoplasmic regions and the cell wall anchor motif are removed from GBS 80. An example of such a GBS 80 fragment is set forth below as **SEQ ID NO: 6**.

SEQ ID NO: 6

MKLKSKLLFSAAVLTMVAGSTVEPVAQFATGMSIVRAAEVVSQERPAKTTVNIYKLQADSYKSEITSNG
GIENKDGEVISNYAKLGDNVKLGQGVQFKRYKVKTDISVDELKKLTTVAAADAKVGTILEEGVSLPQK
TNAQGLVVDALDSKSNVRYLYVEDLKNPSNITKAYAVPFVLELNVANSTGTGFLSEINIYKPNVVD
15 EPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANLGDYKFEITDKFADGLTYKSVGKIKIGSKTLN
RDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGMTLVKNQDALDKATANTDDAAFL EIPVASTIN
EKAVL GKAI ENT FELQYDHT PDKADNP KPSNPPRKPEVHTGGKRFVKKDSTETQTLGGA EFDLLASDG
TAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHDTGTFEIKGLAYAVDANAEGTAVTYKLKETKAPE
GYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTIKNNKRPS

20 Alternatively, in some recombinant host cell systems, it may be preferable to use the cell wall anchor motif to anchor the recombinantly expressed protein to the cell wall. The extracellular domain of the expressed protein may be cleaved during purification or the recombinant protein may be left attached to either inactivated host cells or cell membranes in the final composition.

25 In one embodiment, the leader or signal sequence region, the transmembrane and cytoplasmic regions and the cell wall anchor motif are removed from the GBS 80 sequence. An example of such a GBS 80 fragment is set forth below as **SEQ ID NO: 7**.

SEQ ID NO: 7

30 AEVSQERPAKTTVNIYKLQADSYKSEITSNGGIENKDGEVISNYAKLGDNVKLGQGVQFKRYKVKTDI
SVDELKKLTTVAAADAKVGTILEEGVSLPQKTNAQGLVVDALDSKSNVRYLYVEDLKNPSNITKAYA
VPFVLELNVANSTGTGFLSEINIYKPNVVDPEPKTDKDVKKLGQDDAGYTI GEEFKWFLKSTIPANL
DYKFEITDKFADGLTYKSVGKIKIGSKTLN RDEHYTIDEPTVDNQNTLKITFKPEKFKEIAELLKGM
TLVKNQDALDKATANTDDAAFL EIPVASTINEKAVLGKAI ENT FELQYDHT PDKADNP KPSNPPRKPE
35 VHTGGKRFVKKDSTETQTLGGA EFDLLASDGTAVKWTDALIKANTNKNYIAGEAVTGQPIKLKSHDTG
TFEIKGLAYAVDANAEGTAVTYKLKETKAPEGYVIPDKEIEFTVSQTSYNTKPTDITVDSADATPDTI
KNNKRPS

40 Applicants have identified a particularly immunogenic fragment of the GBS 80 protein. This immunogenic fragment is located towards the N-terminus of the protein and is underlined in the GBS 80 **SEQ ID NO: 2** sequence below. The underlined fragment is set forth below as **SEQ ID NO: 8**.

SEQ ID NO: 2

MKLSKKLLFSAAVLTWVAGSTVEPVAQFATGMSIVRAAEVSOERPAKTTVNIYKLQADSYKSEITTSNG
 GIENKDGVEISNYAKLGDNVKLGQGVQFKRYKVKTDIISVDELKKLTTVEAADAKVGTILEEGVSLPQK
 TNAQGLVVDALDSKSNVRYLYVEDLKNPSNITKAYAVPFVLELPVANSTGTGFLSEINIPKNVVTD
 EPKTDKDVKKLQDDAGYTI GEEFKWFLKSTIPANLGDYEKFEITDKFADGLTYKSVGKIKIGSKTLN
 RDEHYTIDEPTVDNQNTLKITFKPEKFEIAELLKGMTLVKNQDALDKATANTDDAAFLIIPVASTIN
 EKAVLGKAIENITFELYDHTPDKADNPKNPNPRKPEVHTGGKRFVKKDSTETQTLGGAEFDLLASDG
 TAVKWTDALIKANTKNKYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDANAEGTAVTYKLKETKAPE
 GYVIPDKEIETFSVQTSYNTKPTDITVDSADATPDTIKNNKRPSPFNWGGIGTAIFVAIGAAMFAV
 KGMKRRTKDN

SEQ ID NO: 8

AEVSOERPAKTTVNIYKLQADSYKSEITTSNGGIENKDGVEISNYAKLGDNVKLGQGVQFKRYKVKTDI
 SVDELKKLTTVEAADAKVGTILEEGVSLPQKTNAAQGLVVDALDSKSNVRYLYVEDLKNPSNITKAYA
 VPFVLELPVANSTGTGFLSEINIPKNVVTDEPKTDKDVKKLQDDAGYTI GEEFKWFLKSTIPANL
 GDIYEKFEITDKFADGLTYKSVGKIKIGSKTLNRDEHYTIDEPTVDNQNTLKITFKPEKFEIAELLKG

The immunogenicity of the protein encoded by SEQ ID NO: 7 was compared against PBS,
 GBS whole cell, GBS 80 (full length) and another fragment of GBS 80, located closer to the C-
 terminus of the peptide (SEQ ID NO: 9, below).

SEQ ID NO: 9

MTLVKNQDALDKATANTDDAAFLIIPVASTINEKAVLGKAIENITFELYDHTPDKADNPKNPNPRKPEVHTGGK
 RFVKKDSTETQTLGGAEFDLLASDGTAVKWTDALIKANTKNKYIAGEAVTGQPIKLKSHTDGTFEIKGLAYAVDA
 NAEGTAVTYKLKETKAPEGVIPDKEIETFSVQTSYNTKPTDITVDSADATPDTIKNNKRPSPFNWGGIGTAIFVAIGAAMFAV

Both an Active Maternal Immunization Assay and a Passive Maternal Immunization Assay
 were conducted on this collection of proteins.

As used herein, an Active Maternal Immunization assay refers to an *in vivo* protection assay
 where female mice are immunized with the test antigen composition. The female mice are then bred
 and their pups are challenged with a lethal dose of GBS. Serum titers of the female mice during the
 immunization schedule are measured as well as the survival time of the pups after challenge.

Specifically, the Active Maternal Immunization assays referred to herein used groups of four
 CD-1 female mice (Charles River Laboratories, Calco Italy). These mice were immunized
 intraperitoneally with the selected proteins in Freund's adjuvant at days 1, 21 and 35, prior to
 breeding. 6-8 weeks old mice received 20 µg protein/dose when immunized with a single
 antigen, 30-45 µg protein/dose (15 µg each antigen) when immunized with combination of
 antigens. The immune response of the dams was monitored by using serum samples taken on day
 0 and 49. The female mice were bred 2-7 days after the last immunization (at approximately t=
 36 – 37), and typically had a gestation period of 21 days. Within 48 hours of birth, the pups were
 challenged via I.P. with GBS in a dose approximately equal to an amount which would be
 sufficient to kill 70 – 90 % of unimmunized pups (as determined by empirical data gathered from

PBS control groups). The GBS challenge dose is preferably administered in 50 μ l of THB medium. Preferably, the pup challenge takes place at 56 to 61 days after the first immunization. The challenge inocula were prepared starting from frozen cultures diluted to the appropriate concentration with THB prior to use. Survival of pups was monitored for 5 days after challenge.

As used herein, the Passive Maternal Immunization Assay refers to an *in vivo* protection assay where pregnant mice are passively immunized by injecting rabbit immune sera (or control sera) approximately 2 days before delivery. The pups are then challenged with a lethal dose of GBS.

Specifically, the Passive Maternal Immunization Assay referred to herein used groups of pregnant CD1 mice which were passively immunized by injecting 1 ml of rabbit immune sera or control sera via I.P., 2 days before delivery. Newborn mice (24-48 hrs after birth) are challenged via I.P. with a 70 - 90% lethal dose of GBS serotype III COH1. The challenge dose, obtained by diluting a frozen mid log phase culture, was administered in 50 μ l of THB medium.

For both assays, the number of pups surviving GBS infection was assessed every 12 hrs for 4 days. Statistical significance was estimated by Fisher's exact test.

The results of each assay for immunization with SEQ ID NO: 7, SEQ ID NO: 8, PBS and GBS whole cell are set forth in Tables 1 and 2 below.

TABLE 1: Active Maternal Immunization

Antigen	Alive/total	%Survival	Fisher's exact test
PBS (neg control)	13/80	16%	
GBS (whole cell)	54/65	83%	P<0.00000001
GBS80 (intact)	62/70	88%	P<0.00000001
GBS80 (fragment) SEQ ID 7	35/64	55%	P=0.0000013
GBS80 (fragment) SEQ ID 8	13/67	19%	P=0.66

Table 2: Passive Maternal Immunization

Antigen	Alive/total	%Survival	Fisher's exact test
PBS (neg control)	12/42	28%	
GBS (whole cell)	48/52	92%	P<0.00000001
GBS80 (intact)	48/55	87%	P<0.00000001
GBS80 (fragment) SEQ ID 7	45/57	79%	P=0.0000006
GBS80 (fragment) SEQ ID 8	13/54	24%	P=1

As shown in Tables 1 and 2, immunization with the SEQ ID NO: 7 GBS 80 fragment provided a substantially improved survival rate for the challenged pups than the comparison SEQ ID NO: 8 GBS 80 fragment. These results indicate that the SEQ ID NO: 7 GBS 80 fragment may comprise an important immunogenic epitope of GBS 80.

Combinations including GBS 80

The invention includes combinations of two or more GBS antigens wherein the combination includes GBS 80 or a fragment thereof. Applicants have discovered that GBS 80 is particularly suitable for immunization in combination with other GBS antigens and that these antigen

5 combinations provide for a broader coverage among different GBS strains.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

Preferably, the combinations of the invention provide for improved immunogenicity over the
10 immunogenicity of the antigens when administered alone. Improved immunogenicity may be measured, for example, by the Active Maternal Immunization Assay. As discussed above, this assay may be used to measure serum titers of the female mice during the immunization schedule as well as the survival time of the pups after challenge. Preferably, immunization with the immunogenic compositions of the invention yield an increase of at least 2 percentage points (preferably at least 3, 4
15 or 5 percentage points) in the percent survival of the challenged pups as compared to the percent survival from maternal immunization with a single antigen of the composition when administered alone. Preferably, the increase is at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 percentage points. Preferably, the GBS combinations of the invention comprising GBS 80 demonstrate an increase in the percent survival as compared to the percent
20 survival from immunization with a non-GBS 80 antigen alone.

According to one embodiment of the invention, combinations of antigens or fusion proteins containing a portion or portions of the antigens will include GBS 80 or a portion thereof in combination with from one to 10 antigens, preferably one to 10 or less antigens. Such other antigens include by way of example and not limitation, GBS 67, GBS 91, GBS 104, GBS 184, GBS 276, GBS
25 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Still other antigens are identified in U.S. Serial Number 10/415,182, filed April 28, 2003, hereby incorporated in its entirety.

Combinations, for example, can include GBS 80, GBS 104, GBS 322, and GBS 276, ; GBS 80, GBS 338, GBS 330; GBS 80, GBS 330, GBS 104; GBS 80, GBS 104, GBS 404; GBS 80, GBS
30 338, GBS 104; GBS 80, GBS 338, GBS404; GBS 338, GBS 330, GBS 104; GBS 338, GBS 104, GBS 404; GBS 80, GBS 330, GBS 404; GBS 80, GBS 322, GBS 104; GBS 80, GBS 322, GBS 276; GBS 80, GBS 322, GBS 91; GBS 80, GBS 104, GBS 276; GBS 80, GBS 104, GBS 91; GBS 80, GBS 276, GBS 91; GBS 80, GBS 322, GBS 104; GBS 80, GBS 322, GBS 276; GBS 80, GBS 322, GBS 91; GBS 80, GBS 104, GBS 276; GBS 80, GBS 104, GBS 91; GBS 80, GBS 276, GBS 91; GBS 80,
35 GBS 690, GBS 691; GBS 80, GBS 690, GBS 338; GBS 80, GBS 690, GBS 305; GBS 80, GBS 691,

GBS 305; GBS 80, GBS 338, GBS 305; GBS 80, GBS 338, GBS 361; GBS 80, GBS 305, GBS 361; GBS 80, GBS 184, GBS 691; GBS 80, GBS 691, GBS 338; GBS 80, GBS 104, GBS 276, GBS 322; GBS 80, GBS 104, GBS 67, and GBS 322. Examples of combinations of the invention which demonstrate improved immunogenicity are set forth below. A more detailed description of the GBS antigens referred to in these experiments is set forth following the examples.

EXAMPLE 1: Active Maternal Immunization Assay of GBS 80 alone vs. in combination

In this example, the Active Maternal Immunization Assay was used to measure the percent survival of pups challenged with a Type III serotype of GBS (COH1 isolate), at t=56 days. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule discussed above with GBS 80 alone, combinations of GBS antigens (with and without GBS 80), placebo (PBS) or inactivated whole cell GBS isolate as indicated in Table 3 below. In these experiments, the challenge dose for GBS Type III, strain isolate COH1 sufficient to kill 70 – 90 % of unimmunized pups is approximately equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose).

Table 3: Active Maternal Immunization Assay of GBS 80 alone vs. in combination

α -GBS	I Challenge t=56 days Type III COH1 10 x LD 50%	
	Alive/treated	Survival %
α -PBS	3/26	11
α -GBS III	9/20	45
80	24/34	70
80+338+330	39/40	97
80+330+104	38/40	95
80+104+404	24/24	100
80+338+104	33/34	97
80+338+404	30/30	100
338+330+104	22/30	73
338+104+404	24/37	65
80+330+404	25/28	89

As shown in Table 3, combinations of GBS antigens which included GBS 80 demonstrated an improved immunogenicity over the use of the antigens alone. For example, immunization with GBS 80 alone yielded a 70% survival rate among the challenged pups. Immunization with combinations of GBS 80 with GBS 338, GBS 330, GBS 104, and GBS 404 yielded 95 to 100% survival rate among the challenged pups. This is an increase of 25 to 30 percentage points.

By comparison, combinations of these antigens which did not include GBS 80 failed to achieve the % survival of GBS 80 alone. For example, immunization with GBS 338, GBS 104 and

GBS 404 yielded a 65% survival rate. Replacement of any one of these antigens with GBS 80 dramatically increased the percent survival rate to between 97 and 100%. This is an increase of 32 to 35 percentage points. (See percent survival rates of GBS 80, 338, 101 (97%); GBS 80, 338, 404 (100%) and GBS 80, 104, 404 (100%)). Similarly, immunization with GBS 338, 330 and 104 yielded a 73% survival rate. Replacement of any one of these antigens with GBS 80 increased the percent survival rate to between 95 – 97%.

These findings indicate that protection from COH1 isolate is increased with use of GBS 80 in combination with other GBS antigens.

EXAMPLE 2: Active Maternal Immunization Assay of GBS 80, GBS 322, GBS 276, GBS 104 alone vs. in combination

In this example, the Active Maternal Immunization Assay was used to measure the percent survival of pups challenged with a Type III serotype of GBS (COH1 isolate) at t=56 days. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule discussed above with a single GBS antigen, combinations of GBS antigens with GBS 80, and placebo (PBS) as indicated in Table 4 below.

Table 4: Active Maternal Immunization Assay of GBS 80, GBS 322, GBS 276 or GBS 104 alone vs. in combination with GBS 80

α -GBS	I Challenge t=56 days Type III COH1 10x LD 50%	
	Alive/treated	Survival %
80 + 322 + 104	27/27	100
80 + 322 + 276	35/38	92
80 + 322 + 91	24/24	100
80 + 104 + 276	29/30	97
80 + 104 + 91	36/40	90
80 + 276 + 91	33/40	82
GBS 80	24/30	80
GBS 322	7/40	17
GBS 276	13/37	35
GBS 104	28/38	74
α -PBS	2/27	7

As shown in Table 4, the combinations of the antigens with GBS 80 yielded improved immunogenicity over the use of the antigens alone. For example, immunization with GBS 322 alone yielded a 17 % survival rate among the challenged pups. Immunization with combinations of GBS 322 with GBS 80 and another GBS antigen yielded survival rates of 92 – 100%. As another example, immunization with GBS 104 alone yielded a 74% survival rate. Immunization with combinations of

GBS 104 with GBS 80 and another GBS antigen yielded survival rates of 90 – 100%. As another example, immunization with GBS 276 alone yielded a 35% survival rate. Immunization with combinations of GBS 276 with GBS 80 and another GBS antigen yielded survival rates of 82 – 97%.

Having demonstrated the immunogenicity of the above-described combinations, the duration of the immune response in the mouse model was further analysed. The maternal mice used in the above described Active Maternal Immunization Assay were mated a second time and the resulting pups challenged with a different GBS serotype (Type V, CJB 111 isolate) at a dramatically higher dose (300x LD 50%) at t=91 days. The parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. Indication of immunological memory in this model under these conditions is thought to be significant. As shown in Table 5, even under these extreme conditions, increased survival rates were generally achieved, particularly for the combination comprising GBS 80, GBS 322 and GBS 104. It was surprising to note that the percent survival rate for the combination of GBS 80, GBS 233 and GBS 104 was 100% for both the first and second challenges.

Table 5: Second generation pups challenged with higher dose of different strain

α -GBS	II Challenge t=91 days Type V CJB111 300x LD 50%	
	Alive/treated	Survival %
80 + 322 + 104	20/20	100
80 + 322 + 276	32/37	86
80 + 322 + 91	27/30	90
80 + 104 + 276	22/37	59
80 + 104 + 91	36/39	92
80 + 276 + 91	23/28	82
GBS 80	13/30	43
GBS 322	25/30	83
GBS 276	18/40	45
GBS 104	21/39	54
α -PBS	9/36	25

EXAMPLE 3: Active Maternal Immunization Assay of combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, GBS 361 and GBS 184

In this example additional combinations of GBS antigens were used in the Active Maternal Immunization Assay, again with a GBS Type III COH1 isolate challenge. The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combinations of GBS antigens set forth in Table 6 below.

Table 6: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, GBS 361 and GBS 184

α -GBS	I Challenge t=56 days Type III COH1 10x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	26/29	90
80 + 690 + 338	35/40	87
80 + 690 + 305	34/35	97
80 + 691 + 305	37/40	92
80 + 338 + 305	25/30	83
80 + 338 + 361	26/30	87
80 + 305 + 361	23/30	77
80 + 184 + 691	32/39	82
α -PBS	10/40	25

The maternal mice in this model were also mated a second time and the resulting pups challenged with the same GBS isolate at a dramatically higher dose (100x LD 50%) at t=84 days. As in the example above, the parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. As shown in Table 7, even under these extreme conditions, some of the survival rates remained at or above 70%. Surprisingly, the percent survival rates for the combination of GBS 80, GBS 184 and GBS 691 actually increased.

Table 7: Second generation pups challenged with higher dose

α -GBS	II Challenge t=84 days Type III COH1 100x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	19/39	49
80 + 690 + 338	21/30	70
80 + 690 + 305	23/40	57
80 + 691 + 305	22/30	73
80 + 338 + 305	18/30	60
80 + 338 + 361	25/40	62
80 + 305 + 361	21/30	70
80 + 184 + 691	35/40	87
α -PBS	4/20	20

EXAMPLE 4: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305, and GBS 361

In this example additional combinations of GBS antigens were used in the Active Maternal

- 5 Immunization Assay, this time with a GBS Type V, CJB111 isolate challenge. In these experiments, the challenge dose for the GBS Type V, CJB111 isolate sufficient to kill 70 – 90% of unimmunized pups is approximately equal to 60 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combinations of GBS antigens set forth in Table 8 below.
- 10 As shown in Table 8, in this particular challenge study with this specific Type V strain isolate, the survival rates for all of the combinations achieved at least 70%.

Table 8: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 690, GBS 691, GBS 338, GBS 305 and GBS 361

α -GBS	I Challenge t=56 days Type V CJB111 60x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	24/30	80
80 + 690 + 338	11/17	70
80 + 691 + 338	7/10	70
80 + 691 + 305	21/30	70
80 + 338 + 305	26/30	87
80 + 338 + 361	26/30	87
80 + 305 + 361	28/30	93
GBS 80	21/30	70
α -PBS	5/18	28

15

The maternal mice in this model were also mated a second time and the resulting pups challenged with the same GBS isolate at a dramatically higher dose (600x LD 50%) at t=84 days. As in the example above, the parameters of this second, much stronger challenge were outside those of the standard Active Maternal Immunization Assay and were meant to probe the limits of the immunological memory generated from the original maternal immunization in the mouse model. As shown in Table 9, even under these extreme conditions, some of the survival rates remained above 70%. Surprisingly, the percent survival for two of the antigen groups actually increased (GBS 80, GBS 690 and GBS 338) and (GBS 80, GBS 691 and GBS 338).

20

Table 9: Second generation pups challenged with higher dose

α -GBS	II Challenge t=84 days Type V CJB111 600x LD 50%	
	Alive/treated	Survival %
80 + 690 + 691	27/37	73
80 + 690 + 338	15/20	75
80 + 691 + 338	27/30	90
80 + 691 + 305	23/40	57
80 + 338 + 305	12/20	60
80 + 338 + 361	24/30	80
80 + 305 + 361	24/30	80
GBS 80	24/30	80
α -PBS	ND	ND

EXAMPLE 5: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104, GBS 276, and GBS 322

In this example an additional combination of GBS antigens was used in the Active Maternal Immunization Assay, this time with an isolate challenge of different GBS strains. In these experiments, the challenge dose for the different GBS strains was sufficient to kill 60 – 90% of unimmunized pups and is equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the combination of GBS 80 antigen with GBS 104, GBS 276, and GBS 322 antigens in the GBS strains set forth in Table 10 below. Survival % was observed with the GBS combination with two different adjuvants, Alum and Freund's. As shown in Tables 10 and 11, in this particular challenge study, the survival rates for the combination in all of the GBS strains achieved up to 96%.

Table 10: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104, GBS 276, and GBS 322 – Alum adjuvant

ALUM					
Mix=322+80+104+276				PBS	
GBS strains	Type	Alive/treated	Survival %	Alive/treated	Survival %
JM9130013	VIII	32/36	89	18/46	40
CJB111	V	118/145	81	21/110	19
COH1	III	96/115	83	22/104	21
M781	III	42/52	81	18/48	38
2603	V	79/145	54	28/128	22
18RS21	II	86/186	46	24/131	18
DK21	II	31/140	22	28/118	24
7357b –	Ib	25/88	28	25/106	23
A909	Ia	4/40	10	9/60	15
090	Ia	2/31	6	4/53	7
SMO53	VII	17/54	31	4/39	10

5

Table 11: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104, GBS 276, and GBS 322 – Freund adjuvant

Freund					
Mix=322+80+104+276				PBS	
GBS strains	Type	Alive/treated	Survival %	Alive/treated	Survival %
JM9130013	VIII	nd	nd	nd	nd
CJB111	V	47/49	96	12/46	26
COH1	III	47/50	94	12/50	24
M781	III	33/50	66	6/50	12
2603	V	28/30	93	8/48	17
18RS21	II	31/78	40	10/46	22
DK21	II	37/68	54	15/60	25
H36B	Ib	8/38	21	5/60	8
7357b –	Ib	29/50	58	5/50	10
A909	Ia	18/49	37	6/49	12

Accordingly, the invention therefore includes compositions comprising combinations of two or more GBS antigens, wherein the combination includes GBS 80 or a fragment thereof or a

10 polypeptide sequence having sequence identity thereto.

In one embodiment, the combination may consist of two to thirteen GBS antigens, including GBS 80. As an example, the combination may contain GBS 80 and other GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes

GBS 80 in combination with one or more of GBS 104 and GBS 322. For example, the combination may include GBS 80, GBS 104, GBS 322 and GBS 67.

Instead of the full length antigen, the combination may comprise an immunogenic fragment of the selected GBS antigen and/or a polypeptide sequence having sequence identity to the selected antigen.

Preferably, the combination of GBS antigens consists of three, four, five, six, seven, eight, nine, or ten GBS antigens. Still more preferably, the combination of GBS antigens consists of three, four, or five GBS antigens.

Details of examples of GBS antigens for use in combination with GBS 80 are set forth below.

GBS 91

GBS 91 refers to a GBS C3 binding polypeptide. Nucleotide and amino acid sequences of GBS 91 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8937 and SEQ ID 8938. These sequences are set forth below as SEQ ID NOS 10 and 11:

SEQ ID NO. 10

ATGAAAAAAGGACAAGTAAATGATACTAAGCAATCTTACTCTCTACGTAAATATAAAATTTGGTTTAGC
ATCAGTAAATTTAGGGTCATTCAATAATGGTCACAAGTCTGTGTTTTGCGGATCAAACTACATCGGTTT
AAGTTAATAATCAGACAGCCTAGTGTGGATGCTAATAATCTTCCAATGAGACAAGTCGGTCAAGT
GTGATTACTTCCAATAATGATAGTGTTCAGCGCTCGATAAAGTTGTAATAGTCAAAATACGGCAAC
AAAGGACATTACTACTCCTTTAGTAGAGACAAAGCCAATGGTGGAAAAAACATTACCTGAACAGGGA
ATTATGTTTATAGCAAGAAACCGAGGTGAAAAATACACCTTCAAAATCAGCCCCAGTACGTTTCTAT
GCAAGAAGGTGATAAAGTTTCTTATGACCAAGTATTTAATAAAGATAATGTGAAATGGATTTCATA
TAAGTCTTTTTGTGGCGTACGTCGATACGCAGCTATTGAGTCAGTATCCATCAGGAGGTTTCAGAGA
CTAAAGCACCTACTCCTGTAACAAATTCAGGAAGCAATATCAAGAGAAAATAGCAACGCAAGGAAAT
TATACATTTTACATAAAGTAGAAGTAAAAAATGAAGCTAAGGTAGCGAGTCCAACCTCAATTTACATT
GGACAAGGAGACAGAATTTTTTACGACCAAAATACTAATATTGAAGGAAATCAGTGGTTATCTTATA
AATCATTTCAATGGTGTTTCGTCGTTTTGTTTGTAGGTAAAGCATCTTCAGTAGAAAAAATCGAAGAT
AAAGAAAAAGTGTCCTCAACCAAGCCCGTATTACTAAAACCTGGTAGACTGACTATTTCTTAACGA
AACAACACAGGTTTGATATTTTAATTACGAATATTAAGATGATAACGGTATCGTCGCTGTTAAGG
TACCGGTTTGACTGAACAAGGAGGGCAAGATGATATTAATGGTATACAGCTGTAACCTACTGGGGAT
GGCAACTACAAAGTAGCTGTATCAITTTGCTGACCATAAGAATGAGAAGGGTCTTTATAATATTCAATT
ATACTACCAAGAAGCTAGTGGGACACTGTAGGTGTACAGGAACATAAGGTGACAGTAGCTGGAACTA
ATTCTTCTCAAGAACCTATTGAAAATGGTTAGCAAGAGCTGGTCTTTTATATATTTATCGGAAGTACT
GAAGTAAAAAATGAAGCTAAAAATATCAAGTCAGACCCCAATTACTTTAGAAAAAGGTGACAAAAATAA
TTATGATCAAGTATTGACAGCAGATGGTTACCAAGTGGATTCTTACAAATCTTATAGTGGTGTTCGTC
GCTATATTCCTGTGAAAAAGCTTAACACAGTAGTGAAAAAGCGAAAGATGAGGCGACTAAACCGGAT
AGTTATCCCACTTACCTAAACAGGTACCTATACATTTACTAAAACCTGTAGATGTGAAAAAGTCAACC
TAAAGTATCAAGTCAAGTCAAGTAAATTTAATTTTCAAAAGGGTGA AAAAATACATTATGATCAAGTGTAG
TAGTAGATGGTCATCAGTGGATTTCATACAGAGTTATTCCGGTATTCGTCGCTATATTGAAATT

SEQ ID NO. 11

MKKGQVNDTKQSYSLRKYKFLASVILGSFIMVTSVPVFADQTTTSVQVNNQIGTSVDANNSSNETSASS
VITSNNDVQASDKVNSONTATKIDITPLVETKPMVEKLTPEQGNVYVSKETEVENKTPSKSAPVAFY
AKKGDKVFDYQVFNKDNVWKISYKSPCGVRRRYAAIESLDPSGGSETKAPTPVNTSGSNQEKIATQGN
YTFSSHKEVEVNEAKVASPTQFTLDKGDRIFYDQILTIEGNQWLSYKSFNGVRRFVLLGKASSVEKTED
KEKVPSPQPARITKTGRLLTISNETTTGFDILITNIKDNGIAAVKVPVWTEQGGQDDIKWYTAVTGTD

GNKYKAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGKVTVAGTNSSQEPINENGLAKTGVYNIIGST
 EVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKLLTSSSEKAKDEATKPT
 SYPNLPKTGYTFTKTVDVKSQPKVSSPVEFNFQKGEKIHVDQVLVVDGHQWISYKSYSGIRRYIEI

- 5 GBS 91 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 11 above. In one embodiment, one or more amino acids from this leader or signal sequence region of GBS 91 are removed. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 12.

10 **SEQ ID NO: 12**

DQTTSVQVNNQTGTSVDANSSNETSASSVITSNNDSVQASDKVNSQNTATKDITPLVETKPMVEK
 TLPEQGNVYYSKETEVKNTPSKSAPVAFYAKKGDKFYDQVFNKDNVWISYKSYSGVRRYAAIESLD
 PSGGSETKAPTPTVNSGSSNNQEKIATQGNVYTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTI
 EQGQVNVYYSKETEVKNTPSKSAPVAFYAKKGDKFYDQVFNKDNVWISYKSYSGVRRYAAIESLD
 15 NQWLSYKSYSGVRRYFVLLGKASSVEKTEDKEKVSPPQARITKTGRLTISNETTTGFDILITNKKDN
 GIAAVKVPVWTEQGGQDDIKWYTAVTGDDGNYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGK
 VTVAGTNSSQEPINENGLAKTGVYNIIGSTEVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYK
 SYSGVRRYIPVKLLTSSSEKAKDEATKPTSYPNLPKGTGYTFTKTVDVKSQPKVSSPVEFNFQKGEK
 IHDQVLVVDGHQWISYKSYSGIRRYIEI

- 20 GBS 91 contains a C-terminal transmembrane region which may be located within the underlined region near the end of SEQ ID NO: 11 above. In one embodiment, one or more amino acids from the transmembrane and cytoplasmic regions are removed. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 13.

25 **SEQ ID NO: 13**

MKKGQVNDTKQSYSLRKYKGLASVILGSFIMVTSVPFADQTTSVQVNNQTGTSVDANSSNETSASS
 VITSNNDSVQASDKVNSQNTATKDITPLVETKPMVEKTLPEQGNVYYSKETEVKNTPSKSAPVAFY
 AKKGDKFYDQVFNKDNVWISYKSYSGVRRYAAIESLDPSGGSETKAPTPTVNSGSSNNQEKIATQGN
 YTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIENQWLSYKSYSGVRRYFVLLGKASSVEKTED
 30 KEKVSPPQARITKTGRLTISNETTTGFDILITNKKDNGIAAVKVPVWTEQGGQDDIKWYTAVTGDDG
 NYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGKVTVAGTNSSQEPINENGLAKTGVYNIIGST
 EVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKLLTSSSEKAKDEATKPT
 SYPNLPKTG

- 35 GBS 91 contains an amino acid motif indicative of a cell wall anchor: **SEQ ID NO: 14**
 LTKTG (shown in *italics* in SEQ ID NO: 11 above). In one embodiment, both the transmembrane domain and the cell wall anchor motif are removed from GBS 91. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 15.

40 **SEQ ID NO: 15**

MKKGQVNDTKQSYSLRKYKGLASVILGSFIMVTSVPFADQTTSVQVNNQTGTSVDANSSNETSASS
 VITSNNDSVQASDKVNSQNTATKDITPLVETKPMVEKTLPEQGNVYYSKETEVKNTPSKSAPVAFY
 AKKGDKFYDQVFNKDNVWISYKSYSGVRRYAAIESLDPSGGSETKAPTPTVNSGSSNNQEKIATQGN
 YTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILTIENQWLSYKSYSGVRRYFVLLGKASSVEKTED
 45 KEKVSPPQARITKTGRLTISNETTTGFDILITNKKDNGIAAVKVPVWTEQGGQDDIKWYTAVTGDDG
 NYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGKVTVAGTNSSQEPINENGLAKTGVYNIIGST

EVKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYKSYSGVRRYIPVKLLTSSEKAKDEATKPT
SYNP

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane and cytoplasmic regions are removed from the GBS 91 sequence. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 16.

SEQ ID NO: 16

DQTTSVQVNNQTGTSVDANNSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITPLVETKPMVEK
TLPEQGNVYYSKETEVKNTPSKSAPVAFYAKKGDVFDQVFNKDNVWISYKSCGVRYYAAIESLD
PSGGSETKAPTPTVNTSGSNNQEKIATQGNVTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILITIEG
NQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPPQARITKTGRLTISNETTTGFDILITNIKDDN
GIAAVKVPVWTEQGGQDDIKWYTAVTGDNKYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGK
VTAVAGTNSSQEPIENGLAKTGVYNIIGSTEVEKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYK
SYSGVRRYIPVKLLTSSEKAKDEATKPTSYPNLPKTKG

In another embodiment, the leader or signal sequence region, the transmembrane and cytoplasmic regions, and the cell wall anchor motif are all removed from the GBS 91 sequence. An example of such a GBS 91 fragment is set forth below as SEQ ID NO: 17.

SEQ ID NO: 17

DQTTSVQVNNQTGTSVDANNSSNETSASSVITSNNDSVQASDKVVNSQNTATKDITPLVETKPMVEK
TLPEQGNVYYSKETEVKNTPSKSAPVAFYAKKGDVFDQVFNKDNVWISYKSCGVRYYAAIESLD
PSGGSETKAPTPTVNTSGSNNQEKIATQGNVTFSHKVEVKNEAKVASPTQFTLDKGDRIFYDQILITIEG
NQWLSYKSFNGVRRFVLLGKASSVEKTEDKEKVSPPQARITKTGRLTISNETTTGFDILITNIKDDN
GIAAVKVPVWTEQGGQDDIKWYTAVTGDNKYKVAVSFADHKNEKGLYNIHLYYQEASGTLVGVTGK
VTAVAGTNSSQEPIENGLAKTGVYNIIGSTEVEKNEAKISSQTQFTLEKGDKINYDQVLTADGYQWISYK
SYSGVRRYIPVKLLTSSEKAKDEATKPTSYPN

Further information regarding GBS 91 can be found in WO 01/25440 (C3 binding polypeptide), WO 01/32882 (ID-65), WO 02/31156 (BVH) and Reinscheid et al., *Microbiology* (2002) 148: 3245-3254 (*bsp* gene), each of which are incorporated herein by reference in their entirety.

GBS 104

GBS 104 refers to a putative cell wall surface anchor family protein. It has been referred to as *emaA* protein. Nucleotide and amino acid sequences of GBS 104 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8777 and SEQ ID 8778. These sequences are set forth below as SEQ ID NOS 18 and 19:

SEQ ID NO. 18

ATGAAAAAGAGACAAAAAATATGGAGAGGGTTACAGTTACTTTACTAATCCTGTCCCAAAATCCATT
 TGGTATATTGGTACAAGGTGAAACCCAGATACCAATCAAGCACTTGGAAAAAGTAATTTGTTAAAAAAA
 CGGGAGACAAATGCTACACCAATTAGGCAAAAGCGACTTTTGTGTTAAAAAATGACAAATGATAAGTCAGAA
 CCAAGTCACGAAACGGTAGAGGGTTCTGGAGAAGCAACCTTTGAAAAACATAAAACCTGGAGACTACAC
 ATTAAGAGAAGAAACAGCAACCAATTGGTTATAAAAAACTGATAAAACCTGGAAGTTAAAGTTGCAG
 ATAAACGGAGCAACAATAATCGAGGGTATGGATGCAGATAAAGCAGAGAAACGAAAAAGAGTTTGAAT
 GCCCAATATPCCAAAATCAGCTATTATGAGGATACAAAAGAAAAATCCCAATGATTAAATGTAGAGGG
 TTTCCAAGTTTGGTGAACATAACAAGCAATTGAATCCAATAAATGCGAAAAAGATGGTCGAAGAGAGATTG
 CTGAAGGTTGGTTATCAAAAAAATATACAGGGGTCATGATCTCGATAAGAATAAATAAAAAATGAA
 TTTAACTGTTGAGGGTAAAAACCACTGTTGAAACGAAAGAACTTAATCAACCACTAGATGCTGGTGGCT
 ATTAGATATAATCAAAATAGTATGAATAATGAAAGAGCCAATAATTTCTCAAAGAGCAATTAAGAGCTGGGG
 AAGCACTTGAAGAGCTGATTGATAAAATTACATCAAATAAAGACRATAGATAGTCTTTGTGACATAT
 GCCTCAACCAATTTTTGATGGTACTGAAGCGACCGTATCAAAGGGAGTTGCCGATCAAATGGTAAAGC
 GCTGAATGATAGTGATCATGGGATTATCATAAACTACTTTTACAGCAACTACACATAAATTACAGTT
 ATTTAAATTTAACAATAGTGCTAACGAAGTTAATATTTCAAAGTCAAGAATTTCCAAAGGAAGCGGAG
 CATATAAATGGGAGTCGCAACCGCTCTATCAATTTGGTGGCAGACTTACTCAAAAGCTCTAATGAAGC
 AAATGAAATTTTAGAGACAAGAGTTCTAATGCTAGAAAAAACTTATTTTTCAGCTAATGATGGTGG
 TCCCTACGATGTCTTATGCCATAAATTTAATCCTTATATATCAACATCTTACCAAAAACCGATTAAAT
 TCTTTTTTAAATAAATACCAGATAGAAGTGGTATTTCCAGAGAGATTATATAATCAATGGGTGATGA
 TTTATCAAAATAGTAAAGAGAGATGGAGAGAGTTTAACTGTTTCCGATAGAAAAGTTCTCTGTACTG
 GAGGAACGACACAAGCAGCTTATCGAGTACCGCAAAATCAACTCTCTGTATAGTATATGAGGGATAT
 GCAATTAATAGTGGATATTTATCTCTATTGGAGAGATTACAACCTGGGTCATCCATTGATCCCTAA
 GACAAAGAAGTTTCTGCAACGAAACAAATCAAACTCATGGTGAGCCACCAACATTATACCTTTAATG
 GAAATATAAGACCTAAAGGTTATGACATTTTTACTGTTGGGATTTGGTGTAAACGGAGATCCTGGTGCA
 ACTCCTCTTGAAGCTCGAGAAATTTATGCAATCAATATCAAGTAAACAGAAATTTATCAATGTTGA
 TGATACAAATAAAATTTATGATGAGCTAAATAAATCTTTAAACAAATTTGTTGAGGAAAAACATTCTA
 TTGTTGATGGAATGTGACTGATCCTATGGGAGAGATGATTGAATTCGAATTAATAAATGGTCAAAGT
 TTTACACATGATGATTACGTTTTGGTTGGAAATGATGGCAGTCARTTAAAAAATGGTGTGGCTCTGG
 TGGACCAACAGTGTATGGGGGAATTTTAAAGATGTTTACAGTGACTTATGATAAGACATCTCAAACCA
 TCAAAATCAATCAATTTGAACATTAGGAAGTGGCAAAAAGTAGTTCTTACCTATGATGACGTTTAAAA
 GATACTATATAAGTAACAAATTTTACAATACAATAATCGTACACGCTAAGTCCGAAGAGTGAAAA
 AGAACCAAAATATATTCGTGATTTCCCAATTTCCCAAAATTCGTGATGTTCTGTGAGTTTCCGGTACTAA
 CCATCAAGTAATCAGAAAGAAATGGGTGAGGTTGAATTTATTAAGATTAAATAAGACAAACATTCAGAA
 TCGCTTTTGGGAGCTAAGTTTCAACTTCAGATAGAAAAGATTTTTCTGGGTATATAGCAATTTGTTC
 AGAGGGAAGTGATTTACACAAAGAAATGATGGTAAAAATTTTAAAGCACTTCAAGATGGTAACT
 ATAAATATATGAATTTCAAGTCCAGATGGCTATATAGGTTAAACGCAAACTGTTGTGACATTT
 ACAATTCAAAATGGAGAGTTACGAACCTGAAAGCAGATCCAATGCTAATAAATAAATCAATCGGGTA
 TCTTGAAGGAATGGTAAACCTTTATACCAACCTCCCAACCGCCACAGGTGTTTTCTCTAAAA
 CAGGGGGAATTTGGTACAATTTGTCTATATATTAGTTGGTTCTACTTTTATGATACTTACCATTGTTCT
 TTCCGTCGTAAACAATTG

SEQ ID NO. 19

MKKRQKIWRGLSVTLILLSQIPFGLVQGETQDNTQALQKIVIVKKTGDNATPLGKATFVLKNDNDKSE
 TSHETVEGSGEATFENIKPBDYTLREETAPIGYKKTDRKWKVADNGATIIIEGMDADKAEKREKVLN
 AQYPSKAIYEDTKENYPIVNVVEGSKVGEQYKALNPINGKDGRREIAEGWLKKITIGVNDLDKKNYKIE
 LTVEGKTTVETKELNQPLDVVLLDNSNSMNNERNANSQRALKAGEAVEKLIDKITSNKNDRLVITY
 ASTIFDGTETATVSKGVADQNGKALNDSVSWDYHKTTFTATTHNYSYLNLTNDANEVNLKSRIPKEAE
 HINGDRTLYQFGATFTQKALMKANEILETQSSNARKKLIFHVTDGVPTTMSYAINFNFPYISTSYQNQFN
 SFLNKIPDRSGILQBEDFIINGDDYQIVKGDGESEFKLFSRDKVPVTTGGTTQAAYRVPPQNQLSVMSNBEGY
 AINSYIYLYWRDYNWVYFPDPKTKKVSATKQIKITHEGPTTLYFNGNIRPKGYDIFTVGIVGNQDPGA
 TPLEAEKFMQSISSKTENYTNVDDTNKIYDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNQGS

FTHDDYVLVGNDSQLKNGVALGGPNSDGGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLEK
 DNYISNKFYNTNNRTTLPKSEKEPNTIRDFPIPKIRDVREFFVLITISNQKKMGEVEFIKVNKDKHSE
 SLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDGNKYLYEISSPDGYIEVTKPVTTF
 TIQNGEVNTLKA DP NANKNQIGYLEGNGKHLITNTPKRPPGVFPFKTGGIGTIVYILVGSTFMILITICS
 FRRKQL

GBS 104 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO 19 above. In one embodiment, one or more
 amino acid sequences from the leader or signal sequence region of GBS 104 are removed. An
 example of such a GBS 104 fragment is set forth below as SEQ ID NO 20.

SEQ ID NO 20

GETQDTNQA LGKVIVKKTGD NATPLGKATFVLKNDNDKSETSHETVEGSGEATFENIKPGDYTLREET
 APIGYKKTDKTWKVKVADNGATII EGMDADKA EKRKEVLNAQYPSAIYEDTKENYPLVNVGSGKVGE
 QYKALNPINGKDGRRRIAGWLSKKITGVNDL DKNKYKIELTVEGKTTVETKELNQPLDVVLLDNSN
 SMNNERANNSQRALKAGEAVEKLIKITSNKDN RVALVTYASTIFDGT EATVSKGVADQNGKALNDSV
 SWDYHKTTFTATTNYSYLNLTNDANEVNI LKSRIPKEAHEHNGDRTLYQFGATFTQKALMKANEILE
 TQSSNARKKLI FHVTDGVPMTSYAINFNPIYISTSYQNQFNSFLNKIPDRSGILQEDFIINGDDYQIVK
 GDGESFKLFS DRKVPVTGGTQAAYRVPQNQLSVMSNEG YAINSGYIYLWRDYNWVYFPDPKTKKVS
 ATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGI GVGNDPGATPLEAEKFMQSISSKTENYTNVDDTNKI
 YDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQS FTHDDYVLVGNDSQLKNGVALGGPNSD
 GGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLEK DNYISNKFYNTNNRTTLPKSEKEPNTI
 RDPPIPKIRDVREFFVLITISNQKKMGEVEFIKVNKDKHSESLGAKFQLQIEKDFSGYKQFVPEGSDV
 TTKNDGKIYFKALQDGNKYLYEISSPDGYIEVTKPVTTF TIQNGEVNTLKA DP NANKNQIGYLEGNG
 KHLITNTPKRPPGVFPFKTGGIGTIVYILVGSTFMILITICSFRRKQL

GBS 104 contains a C-terminal transmembrane and/or cytoplasmic region which is indicated
 by the underlined region near the end of SEQ ID NO 19 above. In one embodiment, one or more
 amino acids from the transmembrane or cytoplasmic regions are removed. An example of such a
 GBS 104 fragment is set forth below as SEQ ID NO 21.

SEQ ID NO: 21

MKKRQKIWRGLSVTLLILSQIPFGILVQGETQDTNQA LGKVIVKKTGD NATPLGKATFVLKNDNDKSE
 TSHETVEGSGEATFENIKPGDYTLREETAPIGYKKTDKTWKVKVADNGATII EGMDADKA EKRKEVLN
 AQYPSAIYEDTKENYPLVNVGSGKVGEQYKALNPINGKDGRRRIAGWLSKKITGVNDL DKNKYKIE
 LTVGKTTVETKELNQPLDVVLLDNSN SMNNERANNSQRALKAGEAVEKLIKITSNKDN RVALVTY
 ASTIFDGT EATVSKGVADQNGKALNDSVSWDYHKTTFTATTNYSYLNLTNDANEVNI LKSRIPKEA
 HINGDRTLYQFGATFTQKALMKANEILETQSSNARKKLI FHVTDGVPMTSYAINFNPIYISTSYQNQF
 SFLNKIPDRSGILQEDFIINGDDYQIVKGDGESFKLFS DRKVPVTGGTQAAYRVPQNQLSVMSNEG
 AINSGYIYLWRDYNWVYFPDPKTKKVSATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGI GVGNDPGA
 TPLEAEKFMQSISSKTENYTNVDDTNKIYDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQS
 FTHDDYVLVGNDSQLKNGVALGGPNSDGGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLEK
 DNYISNKFYNTNNRTTLPKSEKEPNTIRDFPIPKIRDVREFFVLITISNQKKMGEVEFIKVNKDKHSE
 SLLGAKFQLQIEKDFSGYKQFVPEGSDVTTKNDGKIYFKALQDGNKYLYEISSPDGYIEVTKPVTTF
 TIQNGEVNTLKA DP NANKNQIGYLEGNGKHLITNT

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions are removed. An example of such a GBS 104 fragment is set forth below as SEQ ID NO 22.

SEQ ID NO: 22

GETQDTNQALGKVIKKTGDNATPLGKATFVLKNDNDKSETSHETVEGSGEATFENIKPGDYTLREET
 APIGYKKTDKTKWKVVDNGATIEGMDADKAERKEVLNAQYPKSAIYEDTKENYPLVNVESGKVG
 QYKALNPINGKDGRRRIEAGWLSKKITGVNDLDKNKYKIELTVEGKTTVETKELNQPLDVVVLLDNSN
 SMNNERANNSQALKAGEAVEKLIKITSNKDNRVALVTYASTIPDGTATVSKGVADQNGKALNDVS
 SWDYHKTTFTATTHNYSYLNLTNDANEVNIKLSRIPEAEHINGDRLLYQFGATFTQKALMKANEILE
 TQSSNARKKLI FHVTDGVPMTSYAINFNPYISTSYQNFNSFLNKIPDRSGILQEDDFIINGDDYQIVK
 GDGESFKLPSDRKVPVTTGGTTQAAAYRVPQNQLSVMSNEGAI NSGYI YLYWRDYNWVYPDPKTKKVS
 ATKQIKTHGEPTTLYFNGNIRPKGYDIFTVGIGVNGDPGATPLEAEKFMQSISSTENYTNVDDTNKI
 YDELNKYFKTIVEEKHSIVDGNVTDPMGEMIEFQLKNGQSFTHDDYVLVGNDSQLKNGVALGGPNSD
 GGILKDVTVTYDKTSQTIKINHLNLGSGQKVVLTYDVRLKDNYSNKFYNTNNRTLSPKSEKEPNTI
 RDEFPKIKIRDVREFPVLTISNQKKMGEVEFIKVNKDKHSESLGAKFQLQIEKDFSGYKQFVPEGSDV
 TTKNDGKIYFKALQDGNKYLYEISSPDGYIEVKTTPVVTFTIQNGEVNTLADPNANKNQIGYLEGNG
 KHLITNT

In other embodiments, additional fragments of GBS 104 are provided including an 830 amino acid fragment of GBS 104 of amino acids 28-858, a 359 amino acid fragment of GBS 104 of amino acids 28-387, a 581 amino acid fragment of GBS 104 of amino acids 28-609, or a 740 amino acid fragment of GBS 104 of amino acids 28-768.

GBS 184

GBS 184 refers to a putative lipoprotein. Nucleotide and amino acid sequences of GBS 184 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 1977 and SEQ ID 1978. These sequences are also set forth below as SEQ ID NOS 23 and 24.

SEQ ID NO: 23

ATGAAAAAACAAAACTATTACTGCTTATTGGAGGCTTATTAATAATGATAATGATGACAGCATGTAA
 GGATTCAAAAATCCAGAAAAACCGCACAAAGGAAGAGTACCAAGCTGAACAAAAATTTTAAACCGTTTT
 TTGAGTTTTTAGCACAAAAAGATAAGATTGAGCAAAATACAAAAATACTTACTATTAGTATCGGAT
 TCAGGTGATGCATTAGATTTAGAATATTTCTATAGTATTCAAGATTTAAAAAAAATAAGGATTAGG
 GAAGTTTGAACAAGAAAAAGTCAATAGAAAAGCGGGTGGCTATAATGAGTTAGAAAAATAAGAGG
 TCCATTTTGAATATTTTAAAAATAATATAGTTTATCCAAAAGGAAAAACCGAATATTACATTGATGAC
 TTTATTATCGGAGCAATGGATCTAAAGAATTAAGAATTAAGAAATTAAGTAAAAAGTTATTT
 ATTAAAAACATCCGGAACCTGAGTTGAAGATATAACATATGAATGCCGACACAGTCGAAGCTTATTA
 AAAAA

SEQ ID NO: 24

MKKQKLLLLIGGLLIMIMMTACKDSKIPENRTKEEYQAEQNFKPFPEFLAOKDKDLSKIQYLLLVSD
 SGDALDLEYFYSIQDLKKNKDLGKFETRKSQIEKPGGYNELENKEVPEYFKNNIVYPKGNITPDD
 FTIGAMDTKELKELKKLVKSYLLKHPETELKDITYELPTQSKLIKK

GBS 184 contains a N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO 24, above. In one embodiment, one or more amino acids from the leader or signal sequence are removed from GBS 184. An example of such a GBS 184 fragment is set forth below as SEQ ID NO: 25.

SEQ ID NO: 25

KDSKIPENRTKEEYQAEQNFKPFPEFLAQKDKDLSKIQYLLLVSDSGDALDLEYFYISIQDLKKNKDL
GKFFETRKSQIEKPGGYNELENKEVPEFYFKNNIVYPKGRPNITFDDFDIIGAMDTRELKELKLKVKS
YLLKHPETELKDITYELPTQSKLIKK

GBS 276

GBS 276 refers to a C5a peptidase. Nucleotide and amino acid sequences of GBS 276 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8941 and SEQ ID 8942. These sequences are set forth below as SEQ ID NOS 26 and 27:

SEQ ID NO. 26

TTGCGTAAAAAACAAAACTACCATTTGATAAACTTGCCATTGCGCTTATATCTACGAGCATCTTGCT
CAATGCACAACTCAGACATTAAAGCAAATACTGTGACAGAAAGACACTCCTGCTACCGAACAAAGCCGTAG
AACC CCCACACCAATAGCAGTTTCTGAGGAATCACGATCATCAAAGGAACTAAACCTTCACAACT
20 CCTAGTGATGTAGGAGAAACAGTAGCAGATGACGCTAATGATCTAGCCCTCAAGCTCCTGCTAAAC
TGCTGATACACCAGCAACCTCAAAGCGACTATTAGGGATTGAAACGACCTTCTCATGTCAAAACCC
TGACGAAAAAGCAGGCAAGGGAGCTGGGACCGTTGTCAGTGATTGATGCTGGTTTGTGATAAAAT
CATGAAGCGTGGCGCTTAACAGACAAAATAAAGCAGCTTACCAATCAAAGAAAACTCTGAAAAAGC
TAAAAAGAGCAGCGTATTACCTATGGCGAGTGGGTCAATGATAAGTTGCTTATTACCACGACTATA
25 GTAAAGATGGTAAAAACGCTGTTGATCAAGAACCGGCACACAGTGTCAGGGATCTTGTGAGGAAT
GCTCCTCATCTGAATGAAGAACCTTACCGCCTAGAAGGTGCGATGCCTGAGGCTCAATTGCTTTTGAT
GCGTTCGAAATTTGAAATGGACTAGCAGACTATGCTCGTAACCTACGCTCAAGCTATCAGAGATGCTG
TCACTTTGGGAGCTAAGGTGATTAATATGAGCTTTGGTAATGCTGCATAGCTTACGCCAACCTTCCA
GACGAAACCAAAAAAGCCTTTGACTATGCCAAATCAAAGGTGTTAGCATTGTGACCTCAGCTGGTAA
30 TGATAGTAGCTTTGGGGGCAAGCCCGTCTACCTCTAGCAGATCATCCTGATTATGGGGTGGTGGGA
CACCTGCAGCGGCAGATTCAACATTGACAGTTGCTTCTTACAGCCAGATGAACAGCTCACTGAAACT
GCTACGGTCAAAACAGACGATCATCAAGATAAAGAAATGCCTGTTATTCAACAAACCGTTTGGAGCC
AAACAAGGCTTACGACTATGCTTATGCTAATCGTGGTACGAAGAGGATGATTTAAAGGATGTCGAAG
GTAAGATTGCGCTTATTGAACGTGGCGATATTGATTTCAAAGATAAGATTGCAACCGCTTAAAAAGCT
35 GGTGCTGTAGGGGCTTGATATGACAATCAAGACAAGGGCTTCCGATTGAATTGCCAAATGTTGA
CCAGATGCCTGCGGCCCTTATCAGCTGAAGAGACGGTCTCTTATTAAAGACAATCCCCCAAAACCA
TTACCTTCAATGCGACACCTAAGGTATTGCCAACAGCAAGTGGCACCAAACTAAGCCGCTTCTCAAGC
TGGGGTCTGACAGCTAGCCGCAATATTAAACGGATATTGACGACCCCGGCCAGATATTTGTGCATC
AGTGCTTAACAAAGATATGCCAACTTTCTGGAACCTAGTATGCTGCACCATTTGGTAGCGGTATCA
40 TGGGACTGTGCAAAAGCAATATGAGACACAGTATCCTGATATGACACCATCATGACGCGCTTGTGATTA
GCTAAGAAAGTATTGATGAGCTCAGCAACTGCCCTATATGATGAAGATGAAAAGCTTATTTTCTCC
TCGCCAACAGGGAGCAGGAGCAGTCGATGCTAAAAAGCTTACGACGCAACGATGTATGTAACAGATA
AGGCAATTAACCTCAAGCAAGGTTCACTGAACAATGTTTCTGATAAAATTTGAAGTAACAGTAACAGTT
CACAACAATCTGATAAAGCTCAAGAGTTGATTACCAAGTAACCTGTTCAACACAGATAAAGTATGATGG
45 AAAACACCTTTGCGTTGCTTCCCTAAAGCATTGTATGAGACATCATGGCAAAATACCAATTCAGCGCA
ATAGCAGCAACAAGTCACCGTTCCAACTCGATGCTAGTCGATTTAGCAAGGACTTGCTTGCCAAATG
AAAAATGGCTATTTCTTAGAAGGTTTGTTCGTTTCAACAAAGATCTCAAAAAGAGAGCTTATGAG
CATTTCATATATTTGGTTTCCAGGTGATTTTGGCAATCTGTCAGCTTACGAAAAACCAATCTATGATA

GCAAAGACGGTAGCAGCTACTATCATGAAGCAAATAGTGCCAAAGACCAATTAGATGGTGATGGA
 TTACAGTTTTACGCTCTGAAAAATAACTTTACAGCACTTACCACAGAGTCTAACCCATGGACGATTAT
 TAAAGCTGTCAAAGAAAGGGGTTGAAAAATAGAGGATATCGAATCTTCAGAGATCACAGAAACCATTT
 TTGCAGGTACTTTTGCAAAACAGACGATGATAGCCACTACTATATCCACCGTCACGCTAATGGCAAA
 CCATATGCTGCGATCTCTCCAATGGGGACGGTAACAGAGATTATGTCCAATCCAAGGTACTTTCTTT
 GCGTAATGCTAAAAACCTTGTGGCTGAAGTCTTGGCAAAAGAGGAAATGTTGTTTGGACAAGTGAGG
 TAACCGGAGCAAGTTGTTAAAACTACAACAATGACTTGGCAAGCACACTTGGTTCAACCCGTTTGA
 AAAACGCGTGTGGGACGGTAAAGATAAAGACGGCAAAGTTGTTGCTAACGGAACTTACACCTATCGTGT
 TCGCTAACAGCCGATTAGCTCAGGTGCAAAAGAACACACACTGATTTGATGTGATGTGTAGACAAATA
 CGACACCTGAAGTCGCAACATCGGCAACATTCTCAACAGAAAGATAGTCGTTTGACACTTGCATCTAAA
 CCAAAAACACGACCACCGGTTTACCGTGAGCGTATTGCTTACACTTATATGGATGAGGATCTGCCAAC
 AACAGAGTATATTTCTCCAAATGAAGATGTTACCTTTACTCTTCCCTGAAGAGCGTGAACCAATGGAAG
 GCGCTACTGTTCATTGAAAAATGTCAGACTTTACTTATGTTGTTGAAGATATGGCTGGTAACATCACT
 TATACACCACTGACTAAGCTATTGGAGGGCCACTCTAATAAGCCAGAACAGACGGTTTCAGATCAAGC
 ACCAGACAAGAAACAGAGACTTAAACCCAGAACAGCGGTTACGGTCAACACCCAGATAAAAAAGG
 AACTAAACCCAGAAAAAGATGTTCAAGTCACCAACACAGGTAAACCTCCTCAAAAAGGTCAATCTTCT
 CTTACTCTAGAGAAACGATCTTCTAAGCGTGCTTTAGCTACAAAAGCATCAACAGAGATCAGTTACC
 AAGACTAATGACAAGGATACAAATCGTTTACATCTCCTTAAGTTAGTTATGACCACTTTCTTCTTGG
 GA

SEQ ID NO. 27

MRKKQKLPDKLAIALISTILLSNAQSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQT
 PSDVGETVADDANDLAPQAPAKTADTPATSKATIRDLNDPSHVKTQEKAGAGAGTVVAVIDAGFDKN
 HEAWRLTDKTKARYQSKENLEKAKKEHGIYGEVWVDKVAYYHDYSKDGKNVADQEHGTHVSGILSGN
 APSEMKEPYRLEGAMPEAQLLMRVEIVNGLADYARNYAQAIRDAVNLGAKVINMSFGNAALAYANLP
 DETKKAFFDYAKSKGVSIIVTSAGNDSSFSGGKPRPLADHPDYGUVGTPAAADSTLTVASYSYSPDKQLTET
 ATVKTDHHDQKEMPVISTNRPEFNKAYDYAYANRGTKEDDFKDVGEKIALIERGIDPFKDKIANAKKA
 GAVGLIYDNQDKGFIPLPNVDQMPAAFIISRRDGLLLKDNPKTITFNATPKVLPTASGTCLSRFSS
 WGLTADGNIKPDIAAPGQDILSSVANNKYAKLSGTSMSAPLVAGINGLLQKQYETQYQYPMPTPSERLDL
 AKKVLMSATALYDEDEKAYFSPRQGGAGAVDAKKAASATMYTDEKNTSSKVLHNNVSDKFVETVTV
 HNKSDKPEQELYYQVTVQTDKVDGKHFALAPKALYETSWQKITIIPANSSQVTVPIDASRFSKDLLAQM
 KNGYFLEGFVRFRQDPTKEELMSIPIYIGFRGDFGNLSALEKPIYDSKDGSSYYHEANSDAKDQLDGDG
 LQFYALKNNFTALTTESNFWTIKAVKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGK
 PYAAISPNGDGNRDYVQFGTFLRNAKLNVAEVLDEKGNVVTSEVTEQVVKYNNNDLASTLGSSTRFE
 KTRWDGKDKDKVAVANGTYTYRVRTPISSGAKEQHTDFDVIVDNTTPEVATSATFSTEDSRLLTLASK
 PKTSQPVYRERIATYIMDEDLPTTEYISPNEDGTFLLPEAEATMEGATVPLKMSDFTYVVEDMAGNIT
 YTPVTKLLEBGSNKPQDGSQDQAPDKKPEAKPEQDGSQTPDKKKETKPEKDGSSQTPGKTPQKGQSS
 RTLEKRSKRALATKASTRDQLPTTNDKDTNRLHLHLKLVMTTFFLG

GBS 276 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 27 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 276 are removed. An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 28.

SEQ ID NO: 28

QSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQTPSDVGETVADDANDLAPQAPAKTAD
 TPATSKATIRDLNDPSHVKTLEQKAGKAGTVVAVIDAGFDKNHEAWRLTDKTKARYQSKENLEKAKK
 5 EHGITYGEWVNDKVAAYYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLEGAMPEAQLLLMRV
 EIVNGLADYARNYAQAIRDAVNILGAKVINMSFGNAALAYANLPDETKKAFDYAKSKGVSIVTSAGNDS
 SFGGKRLPLADHPDYGVVGTFAAADSTLTVASYSPDKQLTETATVKTDDHQDKEMPVISTNREEFNK
 AYDYAYANRGTKEDDFKDVEGKIALIERGDIIDFKDKIANAKKAGAVGLIYDNQDKGFPPIELPNVDQM
 PAAFISRRDGLLLKDNPPKTTITFNATPKVLPTASGTKLSRFSSWGLTADGNTKPDIAAPGQDILLSSVA
 10 NNKYAKLSGTSMSAPLVAGIMGLLQKQYETQYVPMTPSERLDLAKKVLMSSTALYDEDEKAYFSRQ
 QGAGAVDAKKAASATMYTVDKDNSTSSKVLNNVSDKFVETVTVHNKSDKPKQELYYQVTVQTDKVDGKH
 FALAPKALYETSWQKITIPANSSKQVTVPIDASRFSKDLAQMKNGYFLEGFVRFKQDPTKEELMSIP
 YIGFRGDFGNLSALEKPIYDSKDGSSYYHEANSDAKDQLDGDGLQFYALKNNTALTITSNFPWTIIKA
 VKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGKPYAAISPNGDGNRDYVQFGGTFLRN
 15 AKNLVAEVLDEKGNVVVTSEVTEQVVKNYNNDLASTLGSTRFEKTRWDGKDKDKGVVANGTYTYRVRY
 TPISSGAKEQHTDFDVI DVNTTPEVATSATFSTEDSRLTLASKPKTSQPVYRERIAITYMDEDLPTTE
 YISPNEDGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNITYTPVTKLELGHNSNKEPQDGSQDAPD
 KPEAKPEQDGSQTPDKKKETKPEKDSGGQTPGKTPQKGQSSRTLKRSSKRALATKASTRDQLPTT
 20 NDKDNTNRLHLLKLVMTTFFLG

GBS 276 contains a C-terminal transmembrane and/or cytoplasmic region which is indicated by the underlined sequence near the end of SEQ ID NO: 27 above. In one embodiment, one or more amino acids from the transmembrane or cytoplasmic regions of GBS 276 are removed. An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 29.

SEQ ID NO: 29

MRKKQKLPFDKLAIALISTISILLNAQSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSSKETKTSQ
 PSDVGETVADDANDLAPQAPAKTADTPATSKATIRDLNDPSHVKTLEQKAGKAGTVVAVIDAGFDKN
 HEAWRLTDKTKARYQSKENLEKAKKEHGITYGEWVNDKVAAYYHDYSKDGKNAVDQEHGTHVSGILSGN
 30 APSEMKEPYRLEGAMPEAQLLLMRVEIVNGLADYARNYAQAIRDAVNILGAKVINMSFGNAALAYANLP
 DETKKAFDYAKSKGVSIVTSAGNDSSFGGKRLPLADHPDYGVVGTFAAADSTLTVASYSPDKQLTET
 ATVKTDHQQDKEMPVISTNREEFNKAYDYAYANRGTKEDDFKDVEGKIALIERGDIIDFKDKIANAKKA
 GAVGVLIDYNQDKGFPPIELPNVDQM PAAFISRRDGLLLKDNPPKTTITFNATPKVLPTASGTKLSRFSS
 WGLTADGNIKPDIAAPGQDILLSSVANNKYAKLSGTSMSAPLVAGIMGLLQKQYETQYVPMTPSERLDL
 35 AKKVLMSSTALYDEDEKAYFSRQQGAGAVDAKKAASATMYTVDKDNSTSSKVLNNVSDKFVETVTV
 HNKSDKPKQELYYQVTVQTDKVDGKH FALAPKALYETSWQKITIPANSSKQVTVPIDASRFSKDLAQM
 KNGYFLEGFVRFKQDPTKEELMSIPYIGFRGDFGNLSALEKPIYDSKDGSSYYHEANSDAKDQLDGDG
 LQFYALKNNTALTITSNFPWTIIKAVKEGVENIEDIESSEITETIFAGTFAKQDDDSHYIHRHANGK
 PYAAISPNGDGNRDYVQFGGTFLRN AKNLVAEVLDEKGNVVVTSEVTEQVVKNYNNDLASTLGSTRFE
 40 KTRWDGKDKDKGVVANGTYTYRVRYTPISSGAKEQHTDFDVI DVNTTPEVATSATFSTEDSRLTLASK
 PKTSQPVYRERIAITYMDEDLPTTEYISPNEDGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNIT
 YTPVTKLELGHNSNKEPQDGSQDAPDKKPEAKPEQDGSQTPDKKKETKPEKDSGGQTPGKTPQKGQSS
 RTLEKRSKRALATK

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions of GBS 276 are removed. An example of such a GBS 276 fragment is set forth below as SEQ ID NO: 30.

SEQ ID NO: 30

QSDIKANTVTEDTPATEQAVEPPQPIAVSEESRSKSKETKTSQTPSDVGETVADDANDLAPQAPAKTAD
 TPATS KATIRDLNDPSHVKTLEKAGKGAGTVVAVI DAGFDKNHEAWRLTDKTKARYQSKENLEKAKK
 EHGIT YGEVWNRKVAIYHDYSKDGKNAVDQEHGTHVSGILSGNAPSEMKEPYRLEGAMPEAQLLLMRV
 5 EIYVGLADYARNYAQAIRDAVNLGAKVINMSFGNAALAYANLPDETKKAFDYAKSGKSVITVSAGNS
 SFGGK PRLPLADHPDYGVVGTAAAADSTLTVASYS PDKQLTETATVKTDDHQDKEMPVI STNRFEPNK
 AYDYA.YANRGTKEDDFDKVEGKIALIERGDIDFKDKIANAKKAGAVGVLIYDNQDKGFPIELPNVDQM
 PAAFI SRRDGLLLKDNPPKTIITFNATPKVLPTASGTKLSRFSSWGLTADGNIKPDIAAPGGQDILSSVA
 NNKYAKLSGTSMASPLVAGIMGLLQKQYETQYPMPTPSERLDLAKKVLMSATALYDEDEKAYFSPRQ
 10 QGAGA VDAKASAAATMYVTDKONTSSKVHLNNVSDKFEVTVTVHNKSDKPKQLYQVTVQTDKVDGKH
 FALAPKALYETSWOKITPI PANSSKQVTVPI DASRFSKDLLAQMKNGYFLEGFVRFKQDPTKEELMSIP
 YIGRGDFGNLSALEKTIPIYDSKDGSSSYHEANS DAKDQLDGDGLQFYALKNNFTALTITTESN PWTIIKA
 VKEGVENIEDIESEITETI FAGTFAKQDDSDHYIIHRHANGKPYAAISPNGDGNRDYVQPGQFLRN
 AKNLVAEVLDKEGNVVVTSEVTEQVVKNNYNDLASTLGSTRFEKTRWDGKDKGKVVANGTYTVRVRY
 15 TPISSGAKEQHTDFDIVDNTTPEVATSATFSTEDSRLTLASKPKTSQPVYERAIYTYMDEDLPTTE
 YISPNEGTFTLPEEAETMEGATVPLKMSDFTYVVEDMAGNIYTPVTKLLEGHNSKPEQDGSQDAPD
 KKPEAKPEQDGSQTPDKKKETKPEKDSGGTQPGKTPQKGQSSRTLEKRSSKRALATK

Further description of GBS 276 can be found in the following references: Qi Chen et al.,

"Immunization with C5a Peptidase or Peptidase-Type III Polysaccharide conjugate Vaccines

Enhances Clearance of Group B Streptococci from Lungs of Infected Mice", Infection and Immunity

(2002) 70 (11):6409 – 6415; Beckmann et al., "Identification of Novel Adhesions from Group B

Streptococci by Use of Phage Display Reveals that C5a Peptidase Mediates Fibronectin Binding"

Infection and Immunity (2002) 70(6):2869 – 2876; Cheng et al., "The Group B Streptococcal C5a

Peptidase Is Both a Specific Protease and an Invasin" Infection and Immunity (2002) 70(5) 2408 –

2413; and Cheng et al., "Antibody against Surface-Bound C5a Peptidase Is Opsonic and Initiates

Macrophage Killing of Group B Streptococci" Infection and Immunity (2001) 69(4):2302 – 2308.

GBS 305

GBS 305 refers to a UDP-N-acetylmuramoylalanine–D-glutamate ligase, also referred to

as Mur D. Nucleotide and amino acid sequences of GBS 305 sequenced from serotype V isolated

strain 2603 V/R are set forth in Ref. 2 as SEQ ID 207 and SEQ ID 208. These sequences are set forth

below as SEQ ID NOS 31 and 32:

SEQ ID NO. 31

ATGGGACGAGTAATGAAACAATAACAACATTTGAAAATAAAAAAGTTTGTAGCTCTGGTTTAGCACG
 ATCTGGAGAGAGCTGCTGCACGTTTGTGTAGCTAAGTTAGGAGCAATAGTGACAGTTAATGATGGCAAAC
 CATTTGATGAAATCCACAGCACAGCTCTTGTGGAAGAGGGTATTAAAGTGGTTTGTGGTAGTCAT
 35 CCTTTAGAAATGTTAGATGAGGATTTTGTGTTACATGATTAAAAATCCAGGAATACCTTATAACAATCC
 TATGGTCAAAAAGCATTAGAAAAACAATCCCTGTTTGTGACTGAAGTGGAAATTAGCATACTAGTTT
 40 CAGAACTCTCAGCTAATAGGTATTACAGGCTCTAACGGGAAACGACAACGACAACGATGATTGCAGAA
 GTCTTAAATGCTGGAGGTCAGAGAGGTTTGTGTAGCTGGGAATATCGGCTTTCCTGCTAGTGAAGTGT
 TCAGGCTCGGAATGATAAGATACTCTAGTTATGGAATATTCAAGTTTTCAGCTAATGGGAGTTAAGG
 AATTTGCTGCTCATATTGCATGATTAATGATTAATGCACTCATGATTAGATTATCATGAGGCTTTT
 GAAGATTATGTGTGTCGAAAATGGAATATCCAAAATCAAATGCTCTCATCTGATTTTTGGTACTTAA
 45 TTTTAATCAAGGTATTCTAAGAGTTAGCTAAACTACTAAGCAACAATCGTTCTTCTCTACTA
 CGGAAAAGTTAGTGGTCTTACGTACAAGCAAGCAACTTTCTATAAAGGGGAGATTTATGAGTCA

GTAGATGACATTGGTGCCAGGAAGCCATAACGTAGAGAATGCTCTAGCAACTATTGCGGTTGCTAA
 ACTGGCTGGTATCAGTAATCAAGTTATTAGAGAACTTTAAGCAATTTTGGAGGTGTTAAACACCGCT
 TGCAATCACTCGGTAAGGTTTCATGGTATTAGTTTCTATAACGACAGCAAGTCAACTAATATATTGGCA
 ACTCAAAAAGCATTATCTGGCTTTGATAATACTAAAGTTATCCTAATTGCAGGAGGTCTTGATCGCGG
 TAATGAGTTTGATGAATTGATACAGATATCACTGGACTTAAACATATGGTTGTTTATAGGGGAATCGG
 CATCTCGAGTAAAACGTGCTGCACAAAAGCAGGAGTAACCTTATAGCGATGCTTTAGATGTTAGAGAT
 GCGGTACATAAAGCTTATGAGGTGGCACAAACAGGGCGATGTTATCTTGCTAAGTCTGCAAAATGCATC
 ATGGGACATGTATAAGAATTTGCAAGTCCGTGGTGATGAATTCATTGATACCTTCGAAAGTCTTAGAG
 GAGAG

SEQ ID NO. 32

MGRVMKTIITTFENKKVLVGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLBEGIKVVCVGS
 HPLELLEDFCYMIKNPGIYPYNNPMVKKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMIAE
 VLNAGGQRLLAGNIGFPASEVVQAANDKDTLMVELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSF
 EDYVAAKWNINQNMSSSDFVLNLFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMS
 VDDIGVPGSHNVENALATIAVAKLAGISNQVIRETLSNFGGVKHLQSLGKVHGISFYNDKSKSTNILA
 TQKALSGFDNTEKIVILIAGGLDRGNEFDELI PDITGLKHMVVLGESASRVKRAAQKAGVITYSDALDVRD
 AVHKAYEVAQQGDVILLSPANASWDMYKNFEVRGDEFIDTFESLRGE

GBS 305 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 32 above. In one embodiment, one or more amino acids from the leader or signal sequence region are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 33.

SEQ ID NO: 33

ITTFENKKVLVGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLBEGIKVVCVGSHPLELLDE
 DFCYMIKNPGIYPYNNPMVKKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMIAEVLNAGGQ
 RGLLAGNIGFPASEVVQAANDKDTLMVELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSFEDYVAAK
 WNIQNMSSSDFVLNLFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMSVDIGV
 PSHNVENALATIAVAKLAGISNQVIRETLSNFGGVKHLQSLGKVHGISFYNDKSKSTNILATQKALSG
 FDDTKVILIAGGLDRGNEFDELI PDITGLKHMVVLGESASRVKRAAQKAGVITYSDALDVRDAVHKAYE
 VAQQGDVILLSPANASWDMYKNFEVRGDEFIDTFESLRGE

GBS 305 contains a C-terminal transmembrane or cytoplasmic region indicated by the underlined sequence near the end of SEQ ID NO: 32 above. In one embodiment, one or more amino acids from the transmembrane or cytoplasmic regions are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 34.

SEQ ID NO: 34

MGRVMKTIITTFENKKVLVGLARSGEAAARLLAKLGAIVTVNDGKPFDENPTAQSLLBEGIKVVCVGS
 HPLELLEDFCYMIKNPGIYPYNNPMVKKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMIAE
 VLNAGGQRLLAGNIGFPASEVVQAANDKDTLMVELSSFQLMGVKEFRPHIAVITNLMPTHLDYHGSF
 EDYVAAKWNINQNMSSSDFVLNLFNQGISKELAKTTKATIVPFSTTEKVDGAYVQDKQLFYKGENIMS
 VDDIGVPGSHNVENALATIAVAKLAGISNQVIRETLSNFGGVKHLQSLGKVHGISFYNDKSK

In one embodiment one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic regions are removed from GBS 305. An example of such a GBS 305 fragment is set forth below as SEQ ID NO: 35.

5 **SEQ ID NO: 35**

ITTFENKKVLVLGLARSGEAAARLLAKLGAI VTVNDGKPFDENPTAQSLLLEEGIKVVCVGSHPLELLDE
DFCYMKIKNGPIYNNPMVKALEKQIPVLTEVELAYLVSESQIGITGSNGKTTTTTMI AEVLNAGGQ
RGLLAGNIGFPASEVVQAANDKDTLVMLSSSFQLMGVKEFRPHIAVITNLMPHTLDYHGSFEDYVAAK
10 WNIQNQMSSSDFLVLNFNQGISKEKAKTTKATIVFPSTTEKVDGAYVQDKQLFFYKGENIMSVDDIGVP
GSHN VENALATTAVAKLAGISNQVIRETLSNFGGVKHRLQSLGKVHGHSFYNDKS

GBS 322

GBS 322 refers to a surface immunogenic protein, also referred to as "sip". Nucleotide and amino acid sequences of GBS 322 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8539 and SEQ ID 8540. These sequences are set forth below as SEQ ID NOS 36 and 37:

SEQ ID NO. 36

ATGAATAAAAAGGTACTATTGACATCGACAATGGCAGCTTCGCTATTATCAGTCGCAAGTGTTCAAGC
20 ACAAGAAAACAGATACGACGCTGGACAGCAGCTACTGTTTCAGAGGTAAGGCGTGATTTGGTAAAGCAAG
ACAAATAATCATCATATACTGTGAAATATGGTGATACACTAAGCGTTATTTCAGAAGCAATGTCAATT
GATA TGAATGTCTTAGCAAAAATAAATAACATTGCAGATATCAATCTTATTTATCCTGAGACAACACT
GACAGTAACTTACGATCAGAAGAGTCATCTGCCACTTCAATGAAAATAGAAACACCGAGCAACAAATG
25 CTGC TGGTCAAAACAACAGCTACTGTGGATTTGAAAACCAATCAAGTTTCTGTGACAGACCAAAAAGTT
TCTC TCAATACAAATTTCCGAAGGTATGACACCAGAAGCAGCAACAACGATTTGTTCCGCAATGAAGAC
ATATTCTTCTGCGCCAGCTTTGAAATCAAAAGAAGTATTAGCACAAGAGCAAGCTGTTAGTCAAGCAG
CAGCTAATGAACAGGTATCACCAGCTCCTGTGAAGTCGATTACTTCAGAAGTTCAGCAGCTAAAGAG
GAAGTTAAACCAACTCAGACGCTCAGTCAGTCAGTCAACAACAGTATCACCAGCTTCTGTTGCCGCTGA
AAACAACGCTCCAGTACGCTAAGTAGCACCGGTAAGAACTGTAGCAGCGCTAGAGTGGCAAGTGTTA
30 AAGTAGTCACTCCTAAAGTAGAACTGGTGCATCACCAGAGCATGTATCAGCTCCAGCAGTTCCTGTG
ACTACGACTTCCAGCTACAGACAGTAAGTTACAAGCGACTGAAGTTAAGAGCGTTCCGGTAGCACAA
AAAA GCTCCAAACAGCAACACCGGTAGCACAAACAGCTTCAACAACAAATGCAGTAGCTGCACATCCTG
AAAA TGCAGGGCTCCAACCTCATGTTGCAGCTTATAAAGAAAAAGTAGCGTCAACTTATGGAGTTAAT
GAATTCAGTACATACCGTCGCGGAGATCCAGGTGATCATGGTAAAGGTTTAGACTTTGACTTTATTTGT
35 AGGTACTAATCAAGCACTTGGTAAATAAAGTTGCACAGTACTCTACACAAAATATGGCAGCAATAACA
TTTCATATGTTATCTGGCAACAAAAGTTTTACTCAAATACAAACAGTATTTATGGACCTGCTAATACT
TGGAA TGCATGCGCAGATCGTGGTGGCGTTACTGCCAACCACTATGACCACGTTACGATCATTTTAA
CAAA TAATATAAAAGGAAGCTATTTGGCTTCTTTTTTATATGCCTTGAATAGACTTTCAAGGTTCT
TATATAATTTTTATTA

SEQ ID NO. 37

MNKKVLLSTMAASLLSVASVQAQETDTTWTARTVSEVKADLVKQDNKSSYTVKYGDTLSVISEAMSI
DMNVLA KINNIADINLIYPETTLTVTYDQKSHATSMKIE TPATNAAGGTTATVDLKTNQVSVADQRV
SLNT I SEGMTPEAATTIVSPMKTYSSAPALKSKEVLAQEQA VSOAAANEQVSPAPVKSI TSEVPAAKE
45 EVKPTQTSVSQSTTSPASVAAETPAVAKVAPVPTVAAPRVASVKVVTTPKVETGASPEHVSAPAVPV
TTTSPATDSKLQATEVKSVPVPAQKAPTAPVAQPASTTNAVAHAHPENAGLQPHVAA YKEKVASTYGVN
EFSTYRAGDPDGHGKLAVDPIGVNTQALGNKVAQYSTQNMANNISYVIWQKQFYSNTNS IYGPANT
WNAMPDRGGVTANHYDHVHVSFNK

GBS 322 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence near the beginning of SEQ ID NO: 37. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 322 are removed. An example of such a GBS 322 fragment is set forth below as SEQ ID NO: 38.

SEQ ID NO: 38

DLVKQDNKSSYTVKYGDLSVISEAMSIDMNVLAKINNIADINLIYPETTLTVTDQKSHSTATSMKIE
 TPATNAAGQTTATVDLKTNQVSVADQKVSINTISEGMTPEAATTIVSPMKTYSSAPALKSKEVLAEQ
 10 AVSQAAANEQVSPAPVKISITSEVPAAKEEVKPTQTSVSQSTTVSPASVAAETPAPVAKVAPVRTVAAP
 RVASVKVVTPKVETGASPEHVSAPAVPVTTTSPATDSKLQATEVKSVPVQAKAPTATPVAQPASTTNA
 VAAHPENAGLQPHVAAYKEKVASTYGVNEFSTYRAGDPGDHGKGLAVDFIVGTNQALGNKVAQYSTQN
 MAANNLSYVIWQQKFYSNTNSIYGPANTWNAMPDRGGVTANHYDHHVHSFNK

GBS 330

GBS 330 refers to a pyruvate kinase, also referred to as "pyk". Nucleotide and amino acid sequences of GBS 330 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8791 and SEQ ID 8792. These sequences are set forth below as SEQ ID NOS 39 and 40:

SEQ ID NO. 39

ATGAATAAACGGGTAAAAATCGTTGCAACACTTGGTCTCGCGTTGAATTCGGTGGTGAAGAAGTT
 TGGTGAGTCTGGATACTGGGGTGAAGCCTTGACGTAGAAGCTTCAGCAGAAAAAATTGCTCAATTGA
 TTAAGAAGGTTGCTAACGTTTTCCGTTTCAACTTCTCACATGGAGATCATGCTGAGCAAGGAGCTCGT
 25 ATGGCTACTGTTTCGTAAGACAGAAGAGATTGCAGGACAAAAAGTTGGCTTCCTCCTTGATACTAAAGG
 ACCTGAAATTCGTACAGAACTTTTTGAAGATGGTGCAGATTTCCATTATATACAACAGGTACAAAAT
 TACGTGTTGCTACTAAGCAAGGTATCAAACTCACTCCAGAAGTGATTGCATTGAATGTTGCTGGTGA
 CTTGACATCTTTGATGACGTTGAAGTTGGTAAGCAAACTCCTGTTGATGATGGTAAACTAGGTCTTAC
 TGTGTTTGCAAAAGATAAAGACACTCGTGAATTTGAAGTAGTTGTTGAGAATGATGGCCTTATTGGTA
 AACAAAAAGGTGTAACATCCCTTATACTAAAATTCCTTTCCAGCAGCTTGCAGAACCGCATATATGCT
 30 GATATCCGTTTTGGCACTTGAGCAAGGACTTAACCTTATTGCTATCTCATTGTACGTACTGCTAAAGA
 TGTAAATGAAGTTCGTGCTATTTGTGAAGAACTGGSMATGGACACGTTAAGTTGTTTGTCTAAAATTG
 AAAATCAACAAGGTATCGATAATATTGATGAGATTATCGAAGCAGCAGATGGTATTATGATTGCTCGT
 GGTGATATGGGTATCGAAGTTCATTGAAATGGTCCAGTTTACCAAAAAATGATCATTACTAAAGT
 TAATGCAGCTGGTAAAGCAGTTATTACAGCAACAATATGCTTGAACAATGACTGATAAACCCACGTG
 35 CGACTCGTTCAAGATATCTGATGTCTTCAATGCTGTTATTGATGGTACTGATGCTACAATGCTTTCA
 GGTGAGTCAGCTAATGGTAAATACCCAGTTGAGTCAGTTTCGTACAAATGGCTACTATTGATAAAAAATGC
 TCAACATTACTCAATGAGTATGGTCGCTTAGACTCATCTGCATTCCCACGTAATAACAAAACCTGATG
 TTATTGCATCTCGCGTTAAGAGATGCAACACACTCAATGGATCAACTTGTGTAACAAATTACTGAA
 ACAGGTAATACAGCTCGTGCCATTTCTAAATCCGTCAGATGCAGACATTTTGGCTGTTACATTTGA
 40 TGAAAAAGTACAACGTTTCATTGATGATTAACTGGGGTGTTATCCCTGTCTTGCAGACAAACAGCAGAT
 CTACAGATGATATGTTTGAAGTTGCAGAACGTGTAGCACTTGAAGCAGGATTTGTTGAATCAGCGCAT
 AATATCGTTATCGTTGCAGGTGTTCTGTAGGTACAGGTGGAACCTAACACAATGCGTGTTCTGTAAGT
 TAAA

SEQ ID NO. 40

MNKRVKIVATLGPAVEFRGGKKFGESGYWGESLDVEASAEKIAQLIKEGANVFRFNFSHGDHAEQGAR
 MATVRKAEELIAGQKVGFFLLDTGKPEIRTELEFDGADFHSTTTGTLKRVATKQIGKSTPEVIALNVAGG
 LDIFDDVEVGKQLVDDGKGLTGVFAKDKDTREFEVVVENDGLIGKQKGVNIPYTKIPFPALAEERDNA
 DIRFGLSEQGLNFIAISFVRTAKDVNEVRAICEETGXGHVKLFAKIEHQQGDINDIDEIERADGIMIR
 GDMGIEVPPEMPVPVYQKMIITKVNAAGKAVITATNMLETMTDKPRATRSEVSDVFNVDGTDTATMLS
 GESANGKYPVESVRTMATIDKNAQTLNNEYGRLDSSAFPRNNKTDVIA SAVKDATHSMDIKLVVTTITE
 TGNTARAI SKFRPDADILAVTFDEKVQRSLMINWGVIPVLADKLPASTDDMFVEVARVALEAGFVESGD
 NIVIVAGVPVGTGGNTNMRVRTVK

GBS 338

GBS 338 refers to a Sat D protein. Nucleotide and amino acid sequences of GBS 338
 sequenced from serotype V isolated strain 2603 V/R arc set forth in Ref. 2 as SEQ ID 8637 and SEQ
 ID 8638. These sequences are set forth below as SEQ ID NOS 41 and 42:

SEQ ID NO. 41

TTGCTCTGCTATAATAGACAAAAAGGTGGTGATATTATGTATTAGCATTAAATCGGTGATATCATTAA
 TTCAAAACAGATACTGAACGTGAAACTTTCCACAGTCTTTTCAGCACTAATGACCGAAGCTATCTG
 ATGTATATGGTGAAGAGCTGATTCTCCATTCACATATTACAGCTGGTGATGAATTTCAAGCTTTATTG
 AAACCATCAAAAAAGGTATTTCAAATTATTGACCATATTCAACTAGCTCTAAAACCTGTTAATGTAAG
 GTTCGGCCTCGGTACAGGAACATTATAACATCCATCAATTCAATGAAAGTATCGGTGCTGATGGTC
 CTGCCACTGCGCATGCTCGCTCAGCTATTAATCATATACATGATAAAATGATTATGGAACAGTTCAA
 TAGCTATTTCGCTTGATGATGAAGACCAAAACCTTGAATTAACACTAAATAGTCTCATTTACAGCTGG
 TGATTTTATCAAGTCAAAATGGACTACAAACCATTTCAAATGCTTGAGCACTTAATACTTCAAGATA
 ATTATCAAGAACATTTCAACATCAAAAGTTAGCCCACTGGAAAAATATTGAACCTAGTGCCTGACT
 AAACGCCTTAAGCAAGCGGCTGAAGATTACTTAAGAACGGAACACAGGCAGCCGACTTATTAGT
 TAAAGTTGCACTCAAACTAAAGGGGGAAGCTATGATTTTC

SEQ ID NO. 42

MSAIIIDKKVVIEMYLALIGDIINSKQILERETFQQS FQQLMTELSDVYGEELISPFTITAGDEFQALL
 KPSKKVFQIIDHIQALAKPVNVRFGLGTGNIITSINSNESIGADGPAYWHARSAINHIHDKNDYGTQVQ
 VAICLDDDEDQNLLETLNLSISAGDFIKSKWTTNNHFQMLEHLILQDNYEQEQFHQKLAQLENIEPSALT
 KRLKASGLKIYLRTQTQADLLVKSCTQTGKGSYDF

GBS 338 may contain an N-terminal leader or signal sequence region which is indicated by
 the underlined sequence at the beginning of SEQ ID NO: 42 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region are removed from GBS 338. An example of
 such a GBS 338 fragment is set forth below as SEQ ID NO: 43.

SEQ ID NO: 43

MYLALIGDIINSKQILERETFQQS FQQLMTELSDVYGEELISPFTITAGDEFQALLKPSKKVFQIIDHI
 IQALAKPVNVRFGLGTGNIITSINSNESIGADGPAYWHARSAINHIHDKNDYGTQVQVAICLDDDEDQNL
 ETLNLSISAGDFIKSKWTTNNHFQMLEHLILQDNYEQEQFHQKLAQLENIEPSALT KRLKASGLKIY
 LRTQTQADLLVKSCTQTGKGSYDF

GBS 361

GBS 361 refers to a *cyII* protein. Nucleotide and amino acid sequences of GBS 361 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8769 and SEQ ID 8770. These sequences are set forth below as SEQ ID NOS 44 and 45:

SEQ ID NO. 44

ATGAGCGTATATGTTAGTGAATAGGAATTATTTCTTCTTTGGGAAAAGAAATTATAGCGAGCATATAACA
GCATCTCTTCCGACTTAAAGAGGAATTTCTAAACATTATATATAAAATCAGCAGCTCTATTTTAGAAT
CTTATACAGGAAGCATAACTAGTGACCCAGAGGTTCTGAGCAATACAAAGATGACAGCAGTAATTTT
10 AAATTTGCTTTTACCGCTTTTGAAGAGGCTCTTGCTTTCTCAGGTGTTAAATTTAAAGCTTATCATAA
TATTGCTGTGTTTTAGGACCTCATTGGGGGAAAGAGTGCTGGTCAAAATGCCTTGTATCAATTTG
AAGAAGGAGAGCGTCAAGTAGATGCTAGTTTATTAGAAAAGCATCTGTTTACCATTATGCTGATGAA
TTGATGGCTTATCATGATATTGTGGGAGCTTCGTATGTTATTTCAACCGCCTGTTCTGCAAGTAATAA
TGCCCTAATATTAGGAACACAATTACTTCAAGATGGCGATTGTGATTTAGCTATTTTGGTGGCTGTG
15 ATGAGTTAAGTGATATTTCTTAGCAGGCTTACATCACTAGGAGCTATTAATACAGAAATGGCATGT
CAGCCCTATTTCTTCTGGAAAAGGAATCAATTTGGGTGAGGGCGCTGGTTTGTGTTCTTGTCAAAGA
TCAGTCCTTAGCTAAATATGAAAAATTTATCCGTGGTCTTATTACTTCAGATGGTTATCATATAACAG
CACCTAAGCAACAGGTGAAGGGGGCGGCACAGATTGCAAGCAGCTAGTGACTCAAGCAGGTATTGAC
TCAGTGAGATTGACTATATTAAACGGTACCGGTACAGGTACTCAAGCTAATGATAAAATGGAAAAAAA
20 TATGTATGGTAAATTTTCCGACAAACGACATTGATCAGCAGTACCAAGGGGCAACGGGTCTACTC
TAGGGGCTGCAGGTATTATCGAATTGATTAAATGTTTAGCGGCAATAGAGGAACAGACTGTACCAGCA
ACTAAAAATGAGATTGGGATAGAAGGTTTCCAGAAAATTTTGTCTATCATCAAAAGAGAGAATACCC
AATAAGAAATGCTTTAAATTTTTCGTTTGTCTTTGGTGGAAATAATAGTGGTGCTCTATTGTCATCTT
TAGATTCACTCTAGAACATTACTGCTAGAGAAAATCTTAAATGGCTATCTTATCATCTGTGTGCT
25 TCCATTTCTAAGAATGAATCACTTCTATTAACCTATGAAAAGTTGCTAGTAATTTCAACGACTTTGA
AGCATTACGCTTTAAAGGGGCTAGACCACCCAAAACGTGTCAACCCAGCACAAATTTAGGAAATGGATG
ATTTTTCCAAAATGGTGCCGTAAACAACAGCTCAAGCACAATAAGAAAGCAATATTAACTAAAAAAA
CAAGATACCTTCAAAGTAGGAATTGTATTTACACACTTCTCGGACCAAGTTGAGGTTGTTGAAGGTAT
TGAAAAGCAAATCAACAAGAGGATATGCACATGTTTCTGCTTACGATTCCCGTTTACAGTAATGA
30 ATGCAGCAGCTGGTATGCTTCTATCATTTTTAAATAACAGGTCTTTATCTGTCAATTTGCACAAAT
AGTGGAGCGCTTGATGGTATACAATATGCCAAGGAAATGATGCGTAACCGATAATCTAGACTATGTGAT
TCTTGTTTCTGCTAATCAGTGGACAGACATGAGTTTTATGTTGGTGGCAACATTAAACATGATAGTC
AAATGTTTGTCCGTTCTGATTATTGTTTACAGCAAGTCCCTCTCTGCTCAAGCATTGATTAATCTCTCT
ATAATATTAGGTAGTAAACAATTAATAATATAGCCATAAAACATTACACAGATGTGATGACTATTTTTGA
35 TGCTGCGCTTCAAATTTTATATCAGACTTAGGACTAACCATAAAGATATCAAGGTTTCTGTTTGA
ATGAGCGGAGAGAGCTAGTTTCAAGATTATGATTTCTTAGCGAACTTGCTGAGTATTATAATATG
CCAACTTCTGCTCTGCTCAGTTTGATTTTTCATCTAATGGTGCTGGTGAAGAACTGGACTATACTGT
TAATGAAAGATAGAAAAGGGCTATTATTATAGTCTTATCTTATCGATCTTGGTGGTATCTCTTTG
CTATTATTGAAAAAGG

SEQ ID NO. 45

MSVYVSGIGIISSLGKNYSEHKQHLFDLKEGISKHLYKNHDSILES YTSITS DPEVPEQYKDETRNF
KFAFTAFEEELASSGVNLKAYHNIAVCLGTS LGGKSAGQNALYQFE EGERQVDASLLEKASVYHIAD E
LMAYHDI V GASYVISTACASNNVILGTQLLDQGDCLALCGCDELSDISLAGFTSLGAINTEMAC
45 QPYSSGKGINLGEAGFVVLVDQSLAKYVKIIGGLITSDGYHITAPKPTGEGAQIAKQLVTOAGID
YSEIDYINGHGTQANDKMEKNMYKFFPTTLLISSTKGQTGHTLGAAGIIEILINCLAAEEQTVPA
TKNEIGIEGFPENFVYHQREYPIRNALNFSFAFGNNSGVLLSSLDSPLETLPARENLMKAILSSVA
SISKNESLSITYEKVANSFNDFEALRFKGRAPKPTVNPQAQFRKMDDFS KMVAVTTAQALIESNLNLLK
QDTSKVGIVTTLSGPVEVVEGLEKQITTEGYAHVASRFFPTVMNAAAGMLSIIIFKITGPLSVISTN
50 SGALDQGYAKEMMRNDNL DYVLVSANQWTDMSFMWWQQLNYDSQMFVGSIDYCAQVLSRQALDNSP

I I L G S K Q I K Y S H K T F T D V M T I F D A A L Q N L L S D L G L T I K D I K G F V W N E R K K A V S S D Y D F L A N L S E Y Y N M P N L A S G Q F G F S S N G A G E E L D Y T V N E S I E K G Y Y L V L S Y I F G G I S F A I E K R

GBS 361 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 45 above. In one embodiment, one or more amino acids from the leader or signal sequence region are removed from GBS 361. An example of such a GBS 361 fragment is set forth below as SEQ ID NO: 46.

SEQ ID NO: 46

V S G I G I I S S L G K N Y S E H K Q H L F D L K E G I S K H L Y K N H D S I L E S Y T G S I T S D P E V P E Q Y K D E T R N F K F A F T A F E E A L A S S G V N L K A Y H N I A V C L G T S L G G K S A G Q N A L Y Q F E E G E R Q V D A S L L E K A S V Y H I A D E L M A Y H D I V G A S Y V I T A C S A S N N A V I L G T Q L L Q D G D C D L A I C G C D E L S D I S L A G T T S L G A I N T E M A C Q P Y S S G K G I N L G E G A G F V V L V D Q S L A K Y G K I I G G L I T S D G Y H I T A P K P T G E G A A Q I A K Q L V T Q A G I D Y S E I D Y I N G H G T G T Q A N D K M E K N M Y K F F P T T L I S S T K G T G H T L G A A G I I E L I N C L A A E E Q T V P A T K N E I G I E G F P E N F V Y H Q K R E Y P I R N A L N F S F A F G G N N S G V L L S S L D S P L E T L P A R E N L K M A I L S S V A S I S K N E S L I S I T Y E K V A S N F N D F E A L R F K G A R P P K T V N P A Q F R K M D D F S K M V A V T T A Q A L I E S N I N L K K Q D T S K V G I V F T T L S G P V E V V E G I E K I T T E G Y A H V S A S R F P P T V M N A A G M L S I I F K I T G P L S V I S T N S G A L D G I Q Y A K E M M R N D N L D V I L V S A N Q W T D M S F M W W Q L N Y D S Q M F V G S D Y C S A Q V L S R Q A L D N S P I I L G S K Q L K Y S H K T F T D V M T I F D A A L Q N L L S D L G L T I K D I K G F V W N E R K K A V S S D Y D F L A N L S E Y Y N M P N L A S G Q F G F S S N G A G E E L D Y T V N E S I E K G Y Y L V L S Y I F G G I S F A I E K R

GBS 404

Nucleotide and amino acid sequences of GBS 404 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8799 and SEQ ID 8800. These sequences are set forth below as SEQ ID NOS 47 and 48:

SEQ ID NO. 47

A T G A A A T A G A T G A C C T A A G A A A A G C G A C A A T G T T G A A G A T C G T C G C T C C A G T A C G C G A G G T T C A T T C T C T A G C G G A G G A A G T G G A T T A C C G A T T C T C A A C T T T T A T G C T G C G A G G A G T T G G A A A A C C A A G C T T G T G G T T T T A A T C A T C T T A C T G C T A C T T G G C G G A G G G G G A C T A A C C A G C A T T T T T A A T G A C T A T C C T C A C C T T C T A G T T A C C A A T C T C A G A A T G T C T C A C G T T C T G T T G A T A A T A G C G C A A C G A G A G A A C A A A T C G A T T T C G T T A A T A A A G T C C T T G G C T C A A C T A G G A T T T C T G G T C A C A A G A A T T C C A A C C C A A G G T T T T G G A A A T T A T A A G G A A C C A A A A C T T G T T C T T A C A C C A A T T C A A T T C A A C A G G T T G T G G T A T A G G T G A A T C T G C T T C A G G A C A T T T T A T T G T T C A G C A G A T A A A A A A A T C T A T C T T G A T A T T C T T T T A C A A T G A A T T A T C A C A T A A A T A T G T G C T A C T G G T G A T T T G C T A T G G C T A C G T C A T C G C C C A C G A A G T T G G T C A C C A C A T T C A A A C A G A G T A G G C A T T A T G A T A A G T A T A T A G A T G C G A C A C G G A C T T A C T A A G A A G A C A A A T G C T T T A A T G T T C G G C T A G A A C T T C A A G C A G A T T A T T A T G C A G G G G T A T G G G C T C A C T A C A T C A G G G A A A A A A T C T C T T A G A A C A A G A G A C T T T G A A G A G G C C A T G A A T G C T G C C C A C G C G C T C G A G A C G A T A C C C T T C A G A A G A A A C C T A C G G A A A A T T A G T G C C T G A T A G C T T T A C C A T G G A A C A G C T G A A C A C G C C A C G T T G T G T T T A A C A A A G G C T T C A A T A T G G T G A C A T C C A A C A C G G T G A T A C T T C T C C G T A G A A C A T C T A

SEQ ID NO. 48

M K I D D L R K S D N V E D R R S S S G G S F S S G G S G L P I L Q L L L L R G S W K T K L V V L I I L L L L G G G L T S I F N D S S S P S S Y Q S Q N V R S V D N S A T R E Q I D F V N K V L G S T E D F W S Q E F Q T Q G F G N Y K E P K L V L Y T N S I Q T G C G I G E S A S G F F Y C S A D K I Y L D I S F Y N E L S H K Y G A T G D F M A V I A H E V G H H I Q T E L G I M P K Y N R M R H L G T K E A N A L N V R L E L Q A D Y Y A G V W A H Y I R G K N L L E Q G D F E E A M N A A H A V G D D T L Q K E T Y G K L V P D S F T H G T A E Q R Q R W F N K G F Q Y G D I Q E H D T F S V E H L

GBS 690

Nucleotide and amino acid sequences of GBS 690 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 9965 and SEQ ID 9966. These sequences are set forth as
 5 SEQ ID NOS 49 and 50 below:

SEQ ID NO. 49

ATGAGTAAACGACAAAATTAGGAATTAGTAAAAAAGGAGCAATTATATCAGGGCTCTCAGTGGCACT
 AATTGTAGTAATAGGTGGCTTTTATGGGTACAATCTCAACCTAATAAGAGTGCAGTAAAACTAACT
 10 ACAAAGTTTTTAAATGTTAGAGAAGGAAGTGTTCCTCCTCAACTCTTTTGACAGGAAAAGCTAAGGCT
 AATCAAGACAGTATGTGTATTTTGTATGCTAATAAAGGTAATCGAGCAACTGTGCAGTTAAAGTGGG
 TGATAAAATCAGACGTGGTCAGCAGTTAGTTCAATATGATACAACAACGTGCACAAGCAGCCTACGACA
 CTGCTAATCGTCAATTAAATAAAGTAGCGCGTCAGATTAATAATCTAAAGACAACAGGAAGTCTTCCA
 15 GCTATGGAATCAAGTGATCAATCTTCTTCATCATCACAAGGACAAGGGACTCAATCGACTAGTGGTGC
 GACGAATCGCTACAGCAAAAATATCAAAAGTCAAGCTAATGCTTCATACAACCAACAACCTTCAAGATT
 TGAATGATGCTTATGCAGATGCACAGGCAGAAGTAAATAAAGCACA AAAAGCATTGAATGATACTGTT
 ATTACAAGTGACGTATCAGGGACAGTTGTTGAAGTTAATAGTGATATTGATCCAGCTTCAAAAACAG
 20 TCAAGTACTTGTCATGTAGCAACTGAAGTAAACTCCAAGTACAGGAACGATGAGTGAGTATGATT
 TGGCTAATGTTAAAAAAGACAGGCTGTTAAAAATAAAATCTAAGGCTCTATCCTGACAAGGAATGGGAA
 GGTAAAAATTCATATATCTCAAATATCCAGAAGCAGAAGCAAAACAATGACTCTAATAACGGCTC
 TAGTGCTGTAATTTATAATATAAAGTAGATATTACTAGCCCTCTCGATGCATTAAAAACAGGTTTTA
 CCGTATCAGTTGAAGTAGTTAATGGAGATAAGCACCTTATTGTCCCTACAAGTTCTGTGATAACAAA
 25 GATAATAAACACCTTTGTTTGGGTATACAATGATTCTAATCGTAAATTTCCAAAGTTGAAGTCAAAAT
 TGGTAAAGCTGATGCTAAGACACAAGAAATTTTATCAGGTTTGAAGCAGGACAAATCGTGGTTACTA
 ATCCAAGTAAACCTTCAAGGATGGGCAAAAATTTGATAATATTGAATCAATCGATCTTAACTCTAAT
 AAGAAATCAGAGGTGAAA

SEQ ID NO. 50

MSKRQNLGISKKGAIISGLSVALIVVIGGLVWVQSPNKS AVKTNKYKVFNVREGSVSSSTLLTGKAKA
 30 NQEQYVYFDANKGNRATVTVKVGDKITAGQQLVQYDTTTAQAA YDTANRQLNKVARQINNLKTTGSLP
 AMESSDQSSSSSQGGTQSTSGATNRLQNYQSQANASYNQQLQDLNDAYADAQAEVNKAQKALNDTV
 ITSDVSGTVVEVNSDIDPASKTSQVLVHVATEGLQVQGTMS EYDLANVKKDQAVIKISKVYPDKWEW
 GKISYISNYPEAEANNNDNNNGSSAVNYKYKVDITSPLDAL KQGFTVSVVEVNGDKHLIVPTSSVINK
 35 DNKHFVWYVNDNRKISKVEVKIKGADAKTQEILSGLKAGQIVVTNP SKTFKDGQKIDNIESIDLNSN
 KKSEVK

GBS 690 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO: 50 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 690 are removed. An example of such
 40 a GBS 690 fragment is set forth below as SEQ ID NO: 51.

SEQ ID NO: 51

FLVWVQSPNKS AVKTNKYKVFNVREGSVSSSTLLTGKAKANQEQYVYFDANKGNRATVTVKVGDKITAG
 QQLVQYDTTAQAA YDTANRQLNKVARQINNLKTTGSLPAMESSDQSSSSSQGGTQSTSGATNRLQ
 45 NYQSQANASYNQQLQDLNDAYADAQAEVNKAQKALNDTVITSDVSGTVVEVNSDIDPASKTSQVLVHV
 ATEGLQVQGTMS EYDLANVKKDQAVIKISKVYPDKWEWKISYISNYPEAEANNNDNNNGSSAVNYK
 YKVDITSPLDAL KQGFTVSVVEVNGDKHLIVPTSSVINKDNKHFVWYVNDNRKISKVEVKIKGADAK
 TQEILSGLKAGQIVVTNP SKTFKDGQKIDNIESIDLNSNKKSEVK

GBS 691

GBS 691 refers to an iron compound ABC transporter, or a substrate binding protein.

Nucleotide and amino acid sequences of GBS 691 sequenced from serotype V isolated strain 2603

V/R are set forth in Ref. 2 as SEQ ID 3691 and SEQ ID 3692. These sequences are set forth as SEQ ID NOS 52 and 53 below:

SEQ ID NO. 52

ATGAAAAAATTGGAATTATTGTCTCACCCTACTGACCTTCTTTTGGTATCTTGCGGACACAAAC
TAAACAAGAAAGCATAAAACAACATTCTTCTAAATGCCTAAATGAAGGCTTACCTATTATGGAA
AAATCTCTGAAAAATCCGAAAAAGTAATTAATTTTACATATTCTTACACTGGGTATTATTAACCTA
GGTGTTAATGTTTCAAGTTACAGTTTAGACTTAGAAAAAGATAGCCCGCTTTTGGTAAACAACGTAA
AGAAGCTAAAAAATTAAGTCTGATGATACAGAGCTATTGCGGCACAAAAACCTGATTTAATCATGG
TTTTCGATCAAGATCCAACATCAATACTCTGAAAAAATTGCAACCACTTTAGTTATTAATATGGT
GCACAAAAATTTATAGATATGATGCCAGCCTTGGGGAAAGTATTCGGTAAAGAAAAAGAGCTAATCA
TGGGTTAGCCAATGGAAAACTAAAACCTCGCTGTCAAAAAAGATTACACCATATCTTAAAGCCTA
ACACTACTTTTACTATTATGGATTTTATGATAAAATATCTATTATATGGTAAATATTTGGACGC
GGTGGAGAACTAATCTATGATTCTAGGTTATGCTGCCCGAGAAAAGTCAAAAAAGATGTCTTTAA
AAAAGGGTGGTTTACCGTTTCGCAAGAAGCAATCGGTGATTACGTTGGAGATTATGCCCTTGTTAATA
TAACCAAAACGACTAAAAAGCAGCTTCATCACTTAAAGAAAGTGATGTCTGGAAGAATTTACAGCT
GTCAAAAAAGGCGACATCATAGAAAGTAACACGACGTGTTTTATTCTCTGACCCCTCTATCTTTAGA
AGCTCAATTAAATCATTTACAAGGCTATCAAAGAAAAATACAAAT

SEQ ID NO. 53

MKKIGIIVLTLLTFFLVSCGQQTQKQESTKTTISKMPKIEGFTYYGKIPENPKKVINFTYSYTGYYLLKL
GVNVSYSYSLDLEKDSFVFGKQLKEAKLTADDTEAIAAQKPDLMVFDQDPNINTLKKIAPTLLVIKYG
AQNYLDMMPALGKVPFKEKEANQWVSQWKTKTLAVKKDLHHILKPNNTTFTIMDFYDKNIYLYGNPFGR
GGELIYDLSGYAAPEKVKKDVFKKGWFTVSQEAIGDYVDYALVNINKTTKKAASSLKESDVWKNLPA
VKKGHIIESNYDVFFSDFLSLEAQLKSFTKAIKENTN

GBS 691 contains an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 53 above. In one embodiment, one or more amino acids are removed from the leader or signal sequence region of GBS 691. An example of such a GBS 691 fragment is set forth below as SEQ ID NO: 54.

SEQ ID NO: 54

EGFTYYGKIPENPKKVINFTYSYTGYYLLKLVNVSYSYSLDLEKDSFVFGKQLKEAKLTADDTEAIAA
QXPDLIMVFDQDPNINTLKKIAPTLLVIKYGAQNYLDMMPALGKVPFKEKEANQWVSQWKTKTLAVKKD
LHHILKPNNTTFTIMDFYDKNIYLYGNPFGRGGELIYDLSGYAAPEKVKKDVFKKGWFTVSQEAIGDYV
GDYALVNINKTTKKAASSLKESDVWKNLPAVKKGHIIESNYDVFFSDFLSLEAQLKSFTKAIKENTN

GBS 691 contains a C-terminal transmembrane or cytoplasmic region which is indicated by the underlined sequence at the end of SEQ ID NO: 53 above. In one embodiment, one or more amino acids are removed from the transmembrane or cytoplasmic region of GBS 691. An example of such a GBS 691 fragment is set forth below as SEQ ID NO: 55.

SEQ ID NO: 55

MKKI G I I V L T L L T F L V S C G Q Q T K Q E S T K T T I S K M P K I E G F T Y Y G K I P E N P K K V I N F T Y S Y T G Y L L K L
G V N V S S Y S L D L E K D S P V F G K Q L K E A K K L T A D D T E A I A A Q K P D L I M V F D Q D P N I N T L K K I A P T L V I K Y G
A Q N Y L D M M P A L G K V F G K E A N Q W S Q W K T K T L A V R K D L H H I L K P N T T F T I M D F Y D K N I Y L Y G N N F G R
G G E L I Y D S L G Y A A P E K V K K D V F K K G W F T V S Q E A I G D Y V G D Y A L V N I N K T T K K A A S S L K E S D V W K N L P A
V K K G H I I E S N Y D V F Y F S D P L S L E A Q L K S F T

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region are removed from GBS 691.

One example of such a GBS 691 fragment is set forth below as SEQ ID NO: 56

SEQ ID NO: 56

E G F T Y Y G K I P E N P K K V I N F T Y S Y T G Y L L K L G V N V S S Y S L D L E K D S P V F G K Q L K E A K K L T A D D T E A I A A
Q K P D L I M V F D Q D P N I N T L K K I A P T L V I K Y G A Q N Y L D M M P A L G K V F G K E A N Q W S Q W K T K T L A V R K D
L H H I L K P N T T F T I M D F Y D K N I Y L Y G N N F G R G G E L I Y D S L G Y A A P E K V K K D V F K K G W F T V S Q E A I G D Y V
G D Y A L V N I N K T T K K A A S S L K E S D V W K N L P A V K K G H I I E S N Y D V F Y F S D P L S L E A Q L K S F T

Additional examples of GBS antigens which may be used in combination with GBS 80 are set forth below.

GBS 4

GBS 4 refers to another putative cell wall surface anchor family protein. Nucleotide and amino acid sequences of GBS 4 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 1 and SEQ ID 2. These sequences are also set forth below as SEQ ID NOS 57 and 58:

SEQ ID NO: 57

A T G A A A G T G A A A A A T A A G A T T T T A A C G A T G G T A G C A C T T A C T G T C T T A A C A T G T G C T A C T T A T T C A T C
A A T C G G T T A T G C T G A T A C A A G T G A T A A G A T A C T G A C A C G A G T G T C G T G A C T A C G A C C T T A T C T G A G G
A G A A A A G A T C A G A T G A A C T A G A C C A G T C T A G T A C T G G T T C T C T C T G A A A A T G A A T C G A G T T C A T C A
A G T G A A C C A G A A A C A A A T C C G T C A A C T A A T C C A C C T A C A A C A G A A C C A T C G C A A C C C T C A C C T A G T G A
A G A G A A C A A G C C T G A T G G T A G A A C G A A G A C A G A A A T T G G C A A T A A T A A G G A T A T T T C T A G T G G A A C A A
A A G T A T T A A T T C A G A A G A T A G T A T T A A G A A T T T A G T A A A G C A A G T A G T G A T C A A G A A G A G T G G A T
C G C G A T G A A T C A T C A T C T T C A A A G C A A A T G A T G G G A A A A A G G C C A C A G T A A G C C T A A A A A G G A A C T
T C C T A A A A C A G G A T A G C C A C T C A G A T A C T G T A A T A G A T C A T C A C G G A G G G A T T A T T C T G T T A T C A T
T A A G T T T T T A C A A T A A G A A A A T G A A C T T T A T

SEQ ID NO: 58

M K V K N K I L T M V A L T V L T C A T Y S S I G Y A D T S D K N T D T S V V T T L S E E K R S D E L D Q S S T G S S S E N E S S S
S E P E T N P S T N P P T E P S Q P S E N K P D G R T K T E I G N N K D I S S G T K V L I S E D S I K N F S K A S S D Q E E V D
R D E S S S S K A N D G K K G S K P K E L P K T G D S H S D T V I A S T G G I I L L S L S F Y N K M K M L Y

GBS 4 contains an N-terminal leader or signal sequence which is underlined at the beginning of SEQ ID NO: 58 above. In one embodiment, one or more amino acids from the N-terminal leader or signal peptide domain of GBS 4 are removed. An example of such a GBS 4 fragment is set forth below as SEQ ID NO 59.

SEQ ID NO 59

DTSDKNTDTSVVTTLSEEKRSDELDQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKP
 DGRKTKEIGNNKDISSGTVLISEDSEIKNFSKASSDQEEVDREDESSSKANDGKKGHGSKPKKELPKTG
 DSHSDTVIASTGGIILLSLSFYNKKMKLY

5

A further N-terminal section of GBS 4 may be removed to facilitate recombinant expression.
 An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 60.

SEQ ID NO: 60

DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKPDGRKTKEIGNNKDISSGTVLISED
 SEIKNFSKASSDQEEVDREDESSSKANDGKKGHGSKPKKELPKTGDSHSDTVIASTGGIILLSLSFYNKK
 MKLY

10

GBS 4 contains an C-terminal transmembrane region which is underlined at the end of SEQ
 ID NO: 58 above. In one embodiment, one or more amino acids from the C-terminal transmembrane
 region is removed. An example of such a GBS 4 fragment is set forth below as SEQ ID NO: 61.

15

SEQ ID NO: 61

MKVKNKILTMVALTVLTCATYSSIGYADTSKNTDTSVVTTLSEEKRSDELDQSSTGSSSENESSSS
 SEPETNPSTNPPTTEPSQSPSEENKPDGRKTKEIGNNKDISSGTVLISEDSEIKNFSKASSDQEEVD
 RDESSSKANDGKKGHGSKPKKE

20

In one embodiment, both the N-terminal leader or signal domain and the C-terminal
 transmembrane domain are removed from the GBS 4 sequence. An example of such a GBS 4
 fragment is set forth below as SEQ ID NO: 62.

25

SEQ ID NO: 62

DTSDKNTDTSVVTTLSEEKRSDELDQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKP
 DGRKTKEIGNNKDISSGTVLISEDSEIKNFSKASSDQEEVDREDESSSKANDGKKGHGSKPKKE

30

In yet another embodiment, the N-terminal leader or signal domain, a further N-terminal
 region and the C-terminal transmembrane domain are removed from the GBS 4 sequence. An
 example of such a GBS 4 fragment is set forth below as SEQ ID NO: 63.

SEQ ID NO: 63

DQSSTGSSSENESSSSSEPETNPSTNPPTTEPSQSPSEENKPDGRKTKEIGNNKDISSGTVLISED
 SEIKNFSKASSDQEEVDREDESSSKANDGKKGHGSKPKKE

35

GBS 22

GBS 22 refers to a putative adhesion lipoprotein. Nucleotide and amino acid sequences of
 GBS 22 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ 8583 and
 SEQ ID 8584. These sequences are set forth below as SEQ ID NOS 64 and 65:

40

SEQ ID NO. 64

ATGAAAGGATACGGAAAGCCTTATTTTTGTCTCGGAGTAGTTACCCATAATTTGCTTATGTGCTTG
TACTAAACAAAGCCAGCAAAAAAATGGCTTGTACGTAGTGACTAGCTTTATTCAGTATATCCATTA
5 CAAAAGCAGTTTCTGGTGATTGATGATATTAATGATTTCAGTACAGTCAGTATTCATGCTTTT
GAACCCCTCATCAAGTGATGTTGCTGCCATTATGATGCTGATCTATTTCTTTATCATTCCGACACACT
AGAAAGCTTGGGCGAGACGTTTGGAAACCTAGTTTGCATCACTCTAAAGTATCTGTAATTGAAGCTTCAA
AAGGTATGACTTTGGATAAAGTTCATGGCTTAGAAGATGTAGAGGCCAGAAAAAGGAGTAGATGAGTCA
ACCTTGATGACCCTCACACTTGGAAATGACCCTGTAAAGATATCTGAGGAAGCACAACCTCATCGCTAC
ACAAATTAGCTAGAAAGGATCCTAAAAACGCTTAAGGTTTATCAAAAAATGCTGATCAAAATTAGTGACA
10 AGGCAATGGCTATTGCAGAGAAGTATAAGCCAAAATTTAAAGCTGCAAAGTCTAAATACTTTGTGACT
TCACATACAGCATTTCTCATACTTAGCTAAGCGATACGGATTGACTCATGAGTATTGCAGGTGCTC
AACCAGCAAGAACCTAGTGCTAAAAAATTAGCCGAAATTCAGGAGTTTGTGAAACCATATAAGGGTTA
AGACTATTTTTGTTGAAGAAGGAGTCTCACCTAAATTAGCTCAAGCAGTAGCTTCAGTACTCGAGTT
AAAAATTGCAAGTTTAAAGTCTTTARAAGCAGTCCCAAAACAAATAAAGATTACTTAGAAAAATTGGA
15 AACTAATCTTAAGGTAAGTCTGTCAAACTGTTAAATCAATAG

SEQ ID NO. 65

MKRIKSLIFVLGVVTLICLCACTKQSQQKNGLSVVTSFYFVYSITKAVSGDLNDIKMIRSQSGIHGF
EPSSSDVAAYIDADLFLYHSHTLEAWARRLEPSLHSHKVSIVIEASKGMLDGVHGLEDVEAEKGVDES
20 TLYDPHTWNPVKVSEEAQLIATQLAKKDPKNAKVYQKNADQFSDKAMAIKPKFKPAKSKYFVT
SHTAFSYLAKRYGLQLGLGAGVSTGEFSPAKKLAEIQEFVKYKVKTI FVEEGVSPKLAQAVASATRV
KIASLSPLXAVPKNNKDYLENLETNLKVLVKSLNQ

GBS 85

25 GBS 85 refers to a putative cell division protein (DivIB). Nucleotide and amino acid
sequences of GBS 85 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as
SEQ ID 215 and SEQ ID 216. These sequences are set forth below as SEQ ID NOS 66 and 67:

SEQ ID NO. 66

ATGCCTAAGAAGAAATCAGATACCCAGAAAAAGAAAGTTGTCTTAAACGGAATGGCAAAAGCGTAA
CCTTGAATTTTTAAAAAAGCAAGAAAGATGAAGAAGAACAAAAACGTATTAAACGAAAAATTACGCT
TAGATAAAGTAAGATAAATTAATATTTCTTCTCTGAAGAACCTCAAAATACACTACTAAATTAAGAAG
CTTCATTTTCCAAAGATTTCAGACCTAAGATTGAAAAGAAACAGAAAAAGAAAAATAGTCAACAG
30 CTTAGCCAAACTAATCGCATTTAGAACTGCACCTATATTGTAGTAGCATTCCTAGTCAATTTAGTTT
CGGTATTCTCTACTAACTCCTTTTAGTAAGCAAAAAACAATAACAGTTAGTGGAAATCAGCATACACCT
GATGATATTTTATAGAGAAAACGAATATCAAAAAACGATATTTCTTTCTTTAATTTTTAAACA
25 TAAAGCTATTGAACAACGTTTATAGCTGCAGAAGATGTATGGGTAAAAACAGCTCAGATGACTTATCAAT
TTCCCAATAAGTTTCATATTCAGTTCAAGAAAATAAGATTATGATATGCACATACAAAGCAAGGA
TATCAACCTGTCTTGGAAAGTGGAAAAAGGCTGATCCTGTAATAGTTTACAGCTACCAAGACACTT
35 CTTAACAATTAACCTTGATAAGGAAGATAGTATTAAGCTATTAAATTAAGATTAAAGGCTTTAGACC
CTGATTTAATAAGTGAGATTGAGGTGATAAGTTTATAGCTGATTCTAAAACGACACCTGACCTCCTGCTG
TAGATATGACGATGGAAATAGTATTAGAATACCATTTATCTAAATTTAAGAAGAGACTTCCTTTTAA
CAAAACAATTAAGAAGAACCTTAAGGAACCTTCTATTGTTGATATGGAAGTGGGAGTTTACACAACAA
CAAAATACCATTGAATCAACCCCTGTTAAAGCAGAAGATACAAAAATAAATCAACTGATAAAACACAA
40 ACACAAATGGTCAGGTTGCGGAAAAATAGTCAAGGACAAACAAATAACTCAAACTACTAATCAACAAGG
ACAACTAGTACACAGAGCAGGCACCTAACCCCTCAAAATGTTAAT

SEQ ID NO. 67

MPKKKSDTPEKEEVVLTEWQKRNLFLKKRKEDBEEQKRINEKLRLDKRSKLNISPEEPQNTTKIKK
50 LHFPIKSRPKIEKKQKKEKIVNSLAKTNIRITAPIFVVAFLVLSVFLLPFFSKQKTIIVSGNQHTP
DDILIEKNTNIQNDYFFSLIFKHKALIEQRLAAEDVWVKTAQMTYQFPNKFHIVQVENKIAYAHKQG

YQPVLETGKKADPVNSSELPKHFLTINLDKEDSIKLLIKDLKALDPDLISEIQVISLADSKTTPDLLL
 LDMHDGNSIRIPLSKFKERLPHYKQIKKNLKEPSIVDMEVGVTNTNTIESTPVKARDTKNKSDDTKQ
 TQNGQVAENSQGGTTNNSNTNQGGQIATEQAPNPQNVN

5 GBS 147

GBS 147 refers to a putative protease. Nucleotide and amino acid sequences of GBS 147 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8525 and SEQ ID 8526. These sequences are set forth below as SEQ ID NOS 68 and 69.

10 SEQ ID NO. 68

GTGGATAAACACTCACTCAAAAAAGGCTATTTTAAAGTTAAACCTTATAACAACTAGTATTTTATTAAT
 GCATAGCAATCAAGTGAATGCAGAGGAGCAAGAATTAAAAACCAAGAGCAATCACCTGTAATTGCTA
 ATGTTGCTCAACAGCCATCGCCATCGGTAACTACTAATACTGTTGAAAAACATCTGTAACAGCTGCT
 TCTGCTAGTAATACAGCGGAAGAATGGGTGATACATCTGTAAAAAATGACAAAACAGAGATGAATT
 15 ATTAGAAGAGTTATCTAAAAACCTTGATACGTCTAATTGGGGGCTGATCTTGAAGAAGATATCCCT
 CTAAACCAGAGACAACCAACAACTAAAGAAAGCAATGTAGTAACAAATGCTTCAACTGCAATAGCACAG
 AAAAGTCCCTCAGCATATGAAGAGGTGAAGCCAGAAAGCAAGTCATCGCTTGCCTGTTCTTGATACATC
 TAAAAATACAAAAATTACAGCCATAACCCAAAGAGGAAAGGGGAAATGTAGTAGCTATTATTGATACATG
 GCTTTGATATTAAACCATGATATTTTCGTTAGATAGCCCAAAGATGATAGACACAGCTTTAAAACT
 20 AAGACAGAATTTGAGGAATTTAAAGCAAAACATAATATCACTTATGGGAAATGGGTAAACGATAAGAT
 TGTTTTGCACATAACTACGCCAACATAACAGAAACGGTGGCTGATATTGCAGCAGCTATGAAAGATG
 GTTATGGTTCAGAAACAAGAATATTTTCGCATGGTACACACGTTGCTGGTATTTTGTAGGTAATAGT
 AAACGTCACGCAATCAATGGTCTTCTTTTGAAGGTGCAGCGCCAAATGCTCAAGTCTTATTAATGCG
 TATTCAGATAAAAATTGATTCGGACAATTTGGTGAAGCATATGCTAAAGCAATCACAGCAGCTGTTA
 25 ATCTAGGAGCAAAAACGATTAAATATGAGTATTGGAAAAACAGCTGATTCTTTAATTCGCTCAATGAT
 AAAGTTAAATTAGCACTTAAATTAGCTTCTGGAAGAGGCGGTGCAGTTGTTGGCTGCCGGAATGA
 AGGCGCAATTTGGTATGGATTATAGCAAAACCATTAACAATACTCCTGACTACGTCAGCGTTAATAGTC
 CAGCTATTTCTGAAGATACTTTGAGTGTGCTAGCTATGAATCACTTAAACTATCAGTGAGGTCGTT
 GAAACCACTATTGAAGGTAACTTAGTTAGTTAGTTCGCGATTGTGACTTCTAAACCTTTTGACAAAGGTAA
 30 GGCCTACGATGTGGTTTATGCAATTTATGGTGCAAAAAAGACTTTGAAGGTAAAGCACTTAAAGGTA
 AGATTGCATTAATTTAGCGTGGTGGTGGACTGATTTTATGACTAAAATCACTCATGCTACAAATGCA
 GGTGTTGTTGGTATCGTTATTTTAAAGATCAAGAAAAACGTGGAAATTTCTCAATTCCTTACCACTGA
 ATTACCTGTGGGATTTATAGTAAAGTAGATGCGAGCGTATAAAAAATCTTCAAGTCAGTTAACAT
 TTAACAGCAGTTTGAAGTAGTTGATAGCCAAAGGTGGTAAATCGTATGCTGGAACAATCAAGTTGGGGC
 35 GTGACAGCTGAAGGAGCAATCAAGCCTGATGTAACAGCTTTCGGCTTTGAAATTTATCTTCAACCTA
 TAATTAATCAATACCAACAATGTCTGGTCAAGTATGGCTTCCACCATGTTGCAGGATTAATGACAA
 TGCTTCAAGTCATTTGCTGAGAAATATAAAGGGATGAATTTAGATTCTAAAAAATTGCTAGAATTG
 TCTAAAAACATCCTCATGAGCTCAGCAACAGCATTATATAGTGAAGAGGTAAGGCGTTTATTCTACC
 ACGTCAGCAAGGTGCAGGTGTAGTTGATGCTGAAAAGCTATCCAGCTCAATATATATTACTGGAA
 40 ACGATGGCAAAAGCTAAAAATTAATCTCAACGAATGGGAGATAAATTTGATATCACAGTTTCAATTCAT
 AAACCTTTAGAGGTGTCAAAGAATTGATTATCAAGCTAATGTAGCAACAGAACAGTAAATAAAGG
 TAAATTTGCCCTTAAACCAACAGCCTTGCTAGATACTAATTGGCAGAAAGTAATTTCTTCGTGATAAAG
 AAACCAAGATTCGATTTTACTATTGATGCTAGTCAATTTAGTCAGAAATTTAAAGAACAGATGGCAAAAT
 GGTATTTCTTGAAGGTTTGTACGTTTAAAGAAGCCAAGGATAGTAATCAGGAGTTAATGAGTAT
 45 TCCTTTCTAGGATTTAATGGTGATTTTGGCAACTTCAAGACACTTGAACACAGATTTATAAGACGC
 TTTCTAAAGGTAGTTTCTACTATAAACCAAAATGATACAACCTATAAAGACCAATTTGGAGTACCAATGAA
 TCAGCTCCTTTTGAAGACCAACACTATACGCTTGTAAACCAATCAGCGCTTTGGGGCTATGTTGA
 TTAATCTCAAAAATGGTGGGGGTTAGAAATTAGCAGCCGAGAGTCAAAAAGAAATTAATTTAGGAACTT
 TTAGAATAAAGGTTGAGGATAAAACAAATCATCTTTTGGAAAGAGATGCAGCGAATCCATATTTT
 50 GCCATTTCTCCAAATAAAGATGGAATAGGACGAAATCACTCCCGGACCACTTTCTTAAGAAATGT
 TAAGGATATTTCTGCTCGAATTTAGATCAAAATGGAATGTTATTTGGCAAGTAAAGTTTATACAT

CTTATCGTAAAAATTCCATAATAATCCAAAGCAAAGTGATGGTCATTATCGTATGGATGCTCTTCAG
 TGGAGTGGT TTAGATAAGGATGGCAAAGTTGTAGCAGATGGTTTTATCTTATCGCTTACGTTACAC
 ACCAGTAGCAGAAAGGAGCAAATAGTCAGGAGTCAGACTTTAAAGTACAAGTAAGTACTAAGTACCCAA
 ATCTTCCTT CACGAGCTCAGTTTGTATGAACTAATCGAACATTAAGCTTAGCCATGCTTAAGGAAAGT
 5 AGTTATGTT CTTACATATCGTTTACAATAGTTTTATCTCATGTTGTAAAGATGAAGAAATAGGGGA
 TCGACCTTCTTACCATTTATTTCCATATAGATCAGAAGGTAAGTGACACTCTCTAAACCGTTAAGA
 TAGGAGAGAGTGAGGTTGCGGTAGACCCCTAAGGCCTTGACACTTGTGTGGAAGATAAAGCTGGTAAT
 TTCGCAACGGTAAAAATTGCTGATCTCTTGAATAAGGCAGTAGTATCAGAGAAAGAAACCGCTATAGT
 AATTCTTAA CAGTTTCAAATATTTTGAATACTTGAAAAAAGAACCTTATTTTATTCTAAAAAGAGAA
 10 AAGTAGTAAACAGAGATCTAGAAGAAATAATATTAGTTAAGCCGCAACACACGTACTACTCAATCA
 TTGCTTAAAGAAATACTAAATCAGGAAATGAGAAAGTCCCTCACTTCTACACCAATAATAGTAGCAG
 AGTAGCTAAGATCATATCACTAAACATAACGGGGATTCTGTTAAACCATACCTTACCTAGTAGTACAG
 ATAGAGCAACGAATGGTCTATTGTTGGTACTTTGGCATTGTTATCTAGTTTACTTCTTTATTGTAAA
 CCAAAAAGACTAAAAATAATAGTAAA

SEQ ID NO. 69

VDKHHSKKA ILKLT LITTS IILMHSNQVNAEEQELKNQE QSPVIANVAQQPSPSVTTNTVEKTSVTTAA
 SASNTAKEMGDTSVKNKDKTEDELLEELSKNLDTSNLGADLEEYPSKPETTNNKESNVVTTNASTAIAQ
 KVPASYEEVVKPESKSSLAVLDTSKITKLQAITQRKGNVVAIIDTGFDINHDI FRLDS PKDDKHSFKT
 20 KTEFEELKAKHNITYGKWVNDKIVFAHNYANNETVADIAAMKDDGYGSEAKNISGHTHVAGI FVGN
 KRPAINGLLLEGAAPNAQVLLMRI PDKIDS DKFGEAYAKAIT DAVNLGAKTINMS IGTADSLIALND
 VKKLALKLASEKGAVVVAAAGNEGAFGMDYSKPLSTNPDYGTVNS PAISED TSLVSASYESLKTISEVV
 ETTIEGKLVKLP I VTSKPF DKGKAYDVVYANYGAKKDFEGKDFPKGKIALIERGGGLDFMTKI THATNA
 GVVGIVIFNDQEKGRNFLI PYRELPVGI I SKVDGERIKNTSSQLTFNQSPFEVVDSQGGNRMLEQSSWG
 25 VTAEGA IKP DVTASGFEIYSSTYNNQYQTMSTGTSMA SPHVAGLMTMLQSHLAEKYKGMNLD SKLLEL
 SKNIMSSATALYSEEDKAFYS PRQQGAGVVD AEKAIQAQYIITGNDGKAKINLKRMGDFKDITVTTH
 KLVEGKVL EYQANVAQVNGKFKLPQALLDTNMQVKVILRDKETQVRFITDASQSKLKEGMAN
 GYFLEGFVR FKEAKDSNQELMS I PFVGFNGDFANLQALETPIYKTL SKGSFYYPKNDTHHKDQLEYNE
 SAPPESSNNY TALLTQASWGVVDYVKNGGELELAPESPKRI ILGT FENKVE DKTHILLERDAANNPYF
 30 AISPNKDGNRDEITPQAFTFLRNVDI SAQVLDQNGVNIWQSKVLPSYRKNFNHNNKQSDGHTYRMDALQ
 WSGLDKDKGVVADGFYTYRLRYTPVAEGANSQESDFKVQVSTKS PNLPSRAQFDETNRTL SLAMPKES
 SYVPTYRLQLVLSHVVKDDEEYGEDTSHYFPHIDQEGKVTL P KTVKIGESEVAVDPKALT LVVEDKAGN
 FATVKLSDLLNAKAVSEKENAIVISNSFKYFDNLKKEPMFISKKEKVVNKNLEEI ILVKPQT VTTTQS
 LSKEITKSGNEKVLSTSTNNNSSRVAKI ISPKHNGDSVNHTLPSTSDRATNGLFVGTGLALLSLLLYLK
 35 PKKTNNNSK

GBS 147 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequence at the beginning of SEQ ID NO 69 above. In one embodiment, one or more
 amino acids from the leader or signal sequence region of GBS 147 are removed. An example of such
 40 a GBS 147 fragment is set forth below as SEQ ID NO: 70.

SEQ ID NO: 70

EEQELKNQE QSPVIANVAQQPSPSVTTNTVEKTSVTTAASASNTAKEMGDTSVKNKDKTEDELLEELSKN
 LDTSNLGADLEEYPSKPETTNNKESNVVTTNASTAIAQKVPASYEEVVKPESKSSLAVLDTSKITKLQAI
 45 TQRKGNVVAIIDTGFDINHDI FRLDS PKDDKHSFKTTEFEELKAKHNITYGKWVNDKIVFAHNYA
 NNETVADIAAMKDDGYGSEAKNISGHTHVAGI FVGN SKRPAINGLLLEGAAPNAQVLLMRI PDKIDS
 DKFGEAYAKAIT DAVNLGAKTINMS IGTADSLIALNDKVKLALKLASEKGAVVVAAAGNEGAFGMDY
 SKPLSTNPDYGTVNS PAISED TSLVSASYESLKTISEVVETTTIEGKLVKLP I VTSKPF DKGKAYDVVYA
 NYGAKKDFE GKD FKGKIALIERGGGLDFMTKI THATNAGVVGIVIFNDQEKGRNFLI PYRELPVGI I
 50 KVDGERIKN TSSQLTFNQSPFEVVDSQGGNRMLEQSSWGVTAEAGAIKPDVTASGFEIYSSTYNNQYQTM
 SGTSMASPHVAGLMTMLQSHLAEKYKGMNLD SKLLELSKNIMSSATALYSEEDKAFYS PRQQGAGV

VDAEKAIQAQYYITGNDGKAKINLKRMDGKDFDITVTIHKLVEGVKELYQYQANVATEQVNVKGFALKPQ
 ALLDNTWQKVIILRDKETQVRFTIDASQFSQKLKEQMANGYFLEGVFRFKEAKDSNQELMSI PFVGFNG
 DFANLQALETPITYKTLKSGSFYYKPNDTTHKDQLEYNESAPFESNNYTALLTQASASWGYVDYVKNNGGE
 5 LELAPESPKRI ILGTFENKVEKDTIHLERDAANNPYFAISPNKDGNRDEITPQATFLRNVKDISAQV
 LDQNGNVIWQSKVLPSYRKNFHNPNKQSDGHYRMDALQWSGLDKDGKVVADGFTYTYRLRYTPVAEGAN
 SQESDFKVQVSTKSNPLPSRAQFDETNRTLSLAMPKESSYVPTYRQLVLSHVVKDEEYGDETSYYHF
 HDQEGKVTLPKTVKIGESEVAVDPKALTLVVEDKAGNFATVKLSDLLNKAVVSEKENAIVISNSFKY
 FDNLKEKPMFISKKEKVNVKNLEETILVKPQTTVTQSLSKETKSGNEKVLSTNNNSSRAKIIISP
 KHNGDSVNHTLPSTSDRATNGLFVGTLLALLSSLLLYLKPKKTKNNNSK

GBS 147 also contains a C-terminal transmembrane and/or cytoplasmic region which may be
 located within the underlined sequence near the end of SEQ ID NO: 69 above. In one embodiment,
 one or more amino acids from the transmembrane and/or cytoplasmic region are removed. An
 example of such a GBS 147 fragment is set forth below as SEQ ID NO: 71.

SEQ ID NO: 71

VDKHHSSKKAILLTLITTSILMHNSQVNAEEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAA
 SASNTAKEMGDTSVKNDKTEDELEELSKNLDTSNLGADLEEEYPSKPEITNNKESNVVNTASTAIAQ
 KVPASAYEEVVKPESKSSLAFLDTSKITKQLQAITQRGKGNVVAIIDTGFDINHDI FRLDSPKDDKHSFKT
 10 KTEFEE LKAKHNITYGKWNVDKI VFAHNYANNDETETVADIAAAMKDGYSSEAKNI SHGTHVAGIFVNGS
 KRPAINGLLLEGAAPNAQVLLMRI PDKIDSDFGEAYAKAITDAVNLGAKTINMSIGKTADSLIAND
 KYKLALKLASEKGVAVVVAAGNEGAFGMDYSKPLSTNPDYGTVNSPAISEDLSVASYESLKTISEVV
 ETTIEGKLVKLPITVTSKPFDKGKAYDVVYANYGAKKDFEGKDFGKIALIERGGGLDFMTKI THATNA
 15 GVVGVIV FNDQEKRGNFLLPYRELPVGI ISKVDGERIKNTSSQITFNQSEFVVDSDQGGNRMLEQSSWG
 VTAEGAIKPDVTSAGFEIYSSTYNNQYQTMSTGSMASPHVAGLMTMLQSHLAEKYKGMNLDSSKKLLEL
 SKNIIIMSSATALYSEEDKAFYSPRQQAGVVDVDAEKAIQAQYYITGNDGKAKINLKRMDGKDFDITVTI
 KLVEGVKELYQYQANVATEQVNVKGFALKPQALLDNTWQKVIILRDKETQVRFTIDASQFSQKLKEQMAN
 20 GYFLEG VFRFKEAKDSNQELMSI PFVGFNGDFANLQALETPITYKTLKSGSFYYKPNDTTHKDQLEYNE
 SAPFESNNYTALLTQASASWGYVDYVKNNGGELELAPESPKRI ILGTFENKVEKDTIHLERDAANNPYF
 AISPKNKDGNRDEITPQATFLRNVKDISAQVLDQNGNVIWQSKVLPSYRKNFHNPNKQSDGHYRMDALQ
 25 WSGLDKDGKVVADGFTYTYRLRYTPVAEGANSQESDFKVQVSTKSNPLPSRAQFDETNRTLSLAMPKES
 SYVPTYRQLVLSHVVKDEEYGDETSYYHFHDQEGKVTLPKTVKIGESEVAVDPKALTLVVEDKAGN
 FATVKLSDLLNKAVVSEKENAIVISNSFKYFDNLKKEKPMFISKKEKVNVKNLEETILVKPQTTVTQSL
 30 LSKETIKSGNEKVLSTNNNSSRAKIIISPKHNGDSVNHT

In one embodiment, one or more amino acids from the leader or signal sequence region and
 one or more amino acids from the transmembrane or cytoplasmic region are removed from the GBS
 147 sequence. An example of such a GBS 147 fragment is set forth below as SEQ ID NO 72.

SEQ ID NO: 72

EEQELKNQEQSPVIANVAQQPSPSVTTNTVEKTSVTAAASNTAKEMGDTSVKNDKTEDELEELSKN
 LDTSNLGADLEEEYPSKPEITNNKESNVVNTASTAIAQKVPASAYEEVVKPESKSSLAFLDTSKITKQLQ
 10 ITQRGKGNVVAIIDTGFDINHDI FRLDSPKDDKHSFKTTEPEELKAKHNITYGKWNVDKI VFAHNYA
 NNTETVADIAAAMKDGYSSEAKNI SHGTHVAGIFVNGSKRPAINGLLLEGAAPNAQVLLMRI PDKIDS
 15 DKFGEAYAKAITDAVNLAGAKTINMSIGKTADSLIANDKVKLALKLASEKGVAVVVAAGNEGAFGMDY
 SKPLSTNPDYGTVNSPAISEDLSVASYESLKTISEVVETTIEGKLVKLPITVTSKPFDKGKAYDVVYA
 NYGAKKDFEGKDFGKIALIERGGGLDFMTKI THATNAGVVGIV FNDQEKRGNFLLPYRELPVGI IS
 20 KVDGERIKNTSSQITFNQSEFVVDSDQGGNRMLEQSSWGVTAEGAIKPDVTSAGFEIYSSTYNNQYQTM
 SGTSMASPHVAGLMTMLQSHLAEKYKGMNLDSSKKLLELSKNIIIMSSATALYSEEDKAFYSPRQQAGV

VDAEKAI QAQYYITGNDGKAKINLKRMDGKFDITVTIHKLVEGVKLEYQANVATEQVNGKGFALKPKQ
 ALLDTNW QKVILRDKETQVRFTIDASQFSQKLKEQMANGYFLEGFVRFKKAKDSNQELMSIPFVGFG
 DFLNLQALLETPIYKLTSLKSGSFYKPNDDTHKDQLEYNESAPFESNNYTALLTQASWSGVYDVKNNGE
 5 LELAPES PKRIILGTFFENKVEDKTIHLLERDAANNPYFAISPNDKGNRDEITPQATFLNRVKDII SAQV
 LDQNGNV IWQSKVLPSYRKNFHNNPKQSDGHYRMDALQWSGLDKDGKVVADGFTYTYRLRYTPVAEGAN
 SQESDFKQVQSTKSPNLPRAQFDETNRTLSLAMPKESYVPTTYRLQVLVSHVVKDEEYGOETSYHYF
 HLDQEGKVLPKTVKIGSEVAVDPKALTLVVEDKAGNFATVKLSDLINKAVVSEKENAIVISNSFKY
 FDNLKE PMFISKKEKVVNKNLEIILVKPQTTVTQTSLSKETKSGNEKVLTSNNNSSRVAKIISP
 KHNGDSVNHT

GBS 173

GBS 173 refers to an amidase family protein. Nucleotide and amino acid sequences of GBS

173 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 8787 and
 SEQ ID 8788. These sequences are set forth below as SEQ ID NOS 73 and 74:

SEQ ID NO. 73

ATGAAACGTAACTACTTTATTCTTAATACGGTGACGGTTTTAACGTTAGCTGCTGCAATGAATACTAG
 CAGTATCTAGTATCTAATAGTACTGAGACAAGTGCTTCAGTAGTTCCTACTACAAATACTATCGTTCAAA
 CTAATGACAGTAATCCTACCGCAAATTTGTATCAGAATCAGGACAATCTGTAATAGTCAAGTAAAA
 20 CCAGATAATTCTGCGGCGCTTACACAGTTGACACGGCTCATCATATTTACGCTCCAGATGCTTTAAA
 AACAACTCAATCAAGTCCTGTCGTTGAGAGTACTTCTACTAAGTTAACTGAAGAGACTTACAAACAAA
 AAGATGGTCAAGATTAGCCACATGGTGAGAAGTGGTCAAGTTACTAGTGAGGAACCTCGTTAATATG
 GCATACGATATTATTGCTAAGAAAAACCACTCTTTAAATGCAGTCATTACTACTAGACGCCAAGAAGC
 TATTGAAGAGGCTAGAAAACTTAAAGATACCAATCAGCCGTTTTAGGTGTTCCCTTGTAGTCAAGG
 25 GGTTAGGCACAGTATTAAAGGTGGTGAACCAATAATGGCTTGATCTATGCAGATGGAAAAATTAGC
 ACATTTGACAGTAGCTATGTCAAAAATATAAGATTAGGATTATTATTTTAGGACAAACGAACTT
 TCCAGAGTATGGGTGGCGTAATATACAGATTCTAAATATATACGGTCTAACGCATAATCCTTGGGATC
 TTGCTCATTAATGCTGGTGGCTCTTCTGGTGGAAGTGCAGCAGCCATTGCTAGCGGAATGACGCCAATT
 30 GCTAGCCGTTAGTGATGCTGGTGGTCTATCCGTATTCATCTTCTTGCACGGGCTTGGTAGGTTTAAA
 ACCAACAAAGAGGATTGGTGAGTAAATGAAAGCCAGATTGCTATAGTACAGCAGTTCAATTTCCATTAA
 CTAAGTCACTAGAGACGCAGAAACATTATTAACCTTATCTAAGAAAAAGCGATCAAACGCTAGTATCA
 GTTAATGATTTAAATCTTTACCAATTGCTTATACCTTTTGAAATCACCAATGGGAACAGAAAGTTAGTCA
 AGATGCTAAAAACCGCTATTATGGACAACGTCACATCTTAAAGAAAAACAGGATTCAAAGTAACAGAGA
 TAGACTTACCAATTGATGGTAGAGCATTAAATGCGTGATTATTCACCTTGGCTATTGGCATGGGAGGA
 35 GCTTTTTCAACAAATTGAAAAAGACTTAAAAAACATGGTTTACTAAGAAGACGCTTGATCCTATTAC
 TTGGCGAGTTCATGTTATTATCAAAATTCAGATAAGGCTGAACCTTAAGAAATCTATTATGGAAAGCCC
 AAAAAATATGGATGATTATCGTAAGGCAATGGAGAGCTTCACAAAGCAATTTCTATTATTTCTTATCG
 CCAACGACCGCAAGTTTAGCCCCCTATAATACAGATCCATATGTAAACAGAGGAGAGATAAAGAGCGCAT
 TTATAATATGGAAACTTAGCCCAAGAAGAAATGCTCTTTAATCGCCAGTGGGAGCCTATGT
 40 TCGGTAGTAACACCTTTTACACAAATTGCTAATATGACAGGACTCCAGCTATCAGTATCCGCACTTAC
 TTATCTGAGTCTGGTTTACCATAGGGACGATGTTAATGGCAGGTGCAACATGATGATGGTATTAAAT
 TAAATTTGCAACTTCTTTGAAAAACATCATGGTTTTAATGTTAAATGTCAGCAAGAAATAATAGATAAG
 AAGTGAACCATCTACTGGCTAATAACAGCCTACTAATCTCCCTCTTTAAAGCTCATTCATCATTAGTA
 AATTAGAAAGAAATTCACAACTTACTCAAGTATCTATCTCAAAAAATGGATGAAATCGTCTGTAA
 45 AATAAACCATCCGTAATGGCATACAAAAAGCACTTCTCAAAACAGTGATACAGAAATCAAGCCCTAT
 CTCAGTTTTAGTAGTAACCCCTTTTATTAGCTTGTGTTAGCTTTTGAACAAAAAGAAATCAGAAAAGT

SEQ ID NO. 74

MKRKYFI LNTVTVLT LAAAMNTSS IYANSTETSASVVP TTTNTIVQ TNDNSNPTAKFVSESGQSVIGQVK
 PNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKLTEETYKQKDGQDLANMVRSGQVTSEELVNM
 AYDIIAKENPNSLNAVITTRRQEAIEEARKLKDNTQPF LGVPLLVKGLGHSIKGGETNNGLIYADGKIS
 TFDSSYVKKYKDLGFIILGQTNFPPEYGWRNITDSKLYGLTHNPWDLAHNAGGSSGGSSAAAIASGMTPI
 ASGSDAGGSIIRIPSSWTGLVGLKPTRGLVSNNEKPDYSYTAHVHFLTKSSRDAETLLTYLKKSDQTLVS
 VNDLKS LPIAYTLKSPMGTEVSDAKNAIMDNVTFLRKQGFVTEIDLPIDGRALMRDYSTLAIGMGG
 AFSTIEKDLKKHGFTEKDVPDITWAVHVIYQNSDKAELKKSIMEAQKHMDYRKAMEKLHKQFPIFLS
 PTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFNROWEPMLRRTPTQIANMTGLPAISIPTY
 LSESLGPIGTMLMAGANYDMVLKIFATFFEKHHGFNVKQRIIDKEVKPSTGLIQPTNSLFAHSSLV
 NLEENSQVTQVSIKKWMKSSVKNKPSVMAYQKALPKTGDESSSLSPVLVVTLLLACFSFVTKKNQKS

GBS 173 contains an N-terminal leader or signal sequence region which is indicated by the
 underlined sequences at the beginning of SEQ ID NO: 74 above. In one embodiment, one or more
 amino acids from the leader or signal sequence of GBS 173 are removed. An example of such a GBS
 173 fragment is set forth below as SEQ ID NO: 75.

SEQ ID NO: 75

TTTNTIVQ TNDNSNPTAKFVSESGQSVIGQVKPDNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKL
 TEETYKQKDGQDLANMVRSGQVTSEELVNMAYDIIAKENPNSLNAVITTRRQEAIEEARKLKDNTQPF LGVPLLVKGLGHSIKGGETNNGLIYADGKISTFDSSYVKKYKDLGFIILGQTNFPPEYGWRNITDSKLYG
 LTHNPWDLAHNAGGSSGGSSAAAIASGMTPIASGSDAGGSIIRIPSSWTGLVGLKPTRGLVSNNEKPDYSYS
 TAVHFLTKSSRDAETLLTYLKKSDQTLVS VNDLKS LPIAYTLKSPMGTEVSDAKNAIMDNVTFLRK
 QGFVTEIDLPIDGRALMRDYSTLAIGMGGAFTIEKDLKKHGFTEKDVPDITWAVHVIYQNSDKAEL
 KKSIMEAQKHMDYRKAMEKLHKQFPIFLSPTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFN
 ROWEPMLRRTPTQIANMTGLPAISIPTYLSESLGPIGTMLMAGANYDMVLKIFATFFEKHHGFNVK
 QRIIDKEVKPSTGLIQPTNSLFAHSSLVNLEENSQVTQVSIKKWMKSSVKNKPSVMAYQKALPKTG
 DESSSLSPVLVVTLLLACFSFVTKKNQKS

GBS 173 may also contain a C-terminal transmembrane and/or cytoplasmic region which
 may be located within the underlined region near the end of SEQ ID NO: 74 above. In one
 embodiment, one or more amino acids from the transmembrane or cytoplasmic region of GBS 173 are
 removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 76.

SEQ ID NO: 76

MKRKYFILNTVTVLT LAAAMNTSS IYANSTETSASVVP TTTNTIVQ TNDNSNPTAKFVSESGQSVIGQVK
 PDNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKLTEETYKQKDGQDLANMVRSGQVTSEELVNM
 AYDIIAKENPNSLNAVITTRRQEAIEEARKLKDNTQPF LGVPLLVKGLGHSIKGGETNNGLIYADGKIS
 TFDSSYVKKYKDLGFIILGQTNFPPEYGWRNITDSKLYGLTHNPWDLAHNAGGSSGGSSAAAIASGMTPI
 ASGSDAGGSIIRIPSSWTGLVGLKPTRGLVSNNEKPDYSYTAHVHFLTKSSRDAETLLTYLKKSDQTLVS
 VNDLKS LPIAYTLKSPMGTEVSDAKNAIMDNVTFLRKQGFVTEIDLPIDGRALMRDYSTLAIGMGG
 AFSTIEKDLKKHGFTEKDVPDITWAVHVIYQNSDKAELKKSIMEAQKHMDYRKAMEKLHKQFPIFLS
 PTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALFNROWEPMLRRTPTQIANMTGLPAISIPTY
 LSESLGPIGTMLMAGANYDMVLKIFATFFEKHHGFNVKQRIIDKEVKPSTGLIQPTNSLFAHSSLV
 NLEENSQVTQVSIKKWMKSSVKNK

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region are removed. An example of such a GBS 173 fragment is set forth below as SEQ ID NO: 77.

5 **SEQ ID NO: 77**

TTNTIIVQTNDNSNPTAKFVSESQGSVIGQVKPDNSAALTTVDTPHHISAPDALKTTQSSPVVESTSTKL
TEETYKQKNGQDLANMVRSGQVTSEELVNMAVDI IAKENPSLNAVITTRROEAEIEEARKLKDNTQNPFL
GVPELLVQGLGHSIKGGETNNGLIYADGKISTFDSYVVKYKDLGFIIILGQTNFPFYGRWNITDSKLYG
LTHNPWDLAHNAGSSGSGSAAAIASGMTPIASGSDAGGSI RIPSSWTGLVGLKPTRGLVSNNEKPDYS
10 TAVHFPLTKSSRDAETLLTYLKKSDOTLVSVNDLKSLP IAYTLKSPMGTEVVSQDAKNAIMDNVTFLEK
QGFYKTEI DLPIDGRALMRDYSTLAIGMGGAFTIEKDLKKHGFTKEVDVPTTWAVEVVIYQNSDKAEL
KKSIMEAQKHMDYRKAMEKLHKQFP IFLSPPTTASLAPLNTDPYVTEEDKRAIYNMENLSQEERIALF
NRQWEPMLRRTPTPTQIANMTGLPAISIPTYLSESGLP IGTMLMAGANYDMVLKIFATFFFEKHHGFNVK
WQRIIDKEVKPSTGLIQPTNSLFKAHSSLVNLEENSQVTQVSI SKKWMKSSVKNK

15 **GBS 313**

Nucleotide and amino acid sequences of GBS 313 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 4089 and SEQ ID 4090. These sequences are set forth as SEQ ID NOS 78 and 79 below:

20 **SEQ ID NO. 78**

ATGAAACGTTATGCTGTTTAACTAGTGGTGGTGACGCCCTGGTATGAACGCTGCTATCCGTGCAGT
TGTTTCGTAAGCAATTTCTGAAGGTATGGAAGTTTACGGCATCAACCAAGGTACTATGGTATGGTGA
CAGGGGATATTTTCCCTTTGGATGCTAATTTCTGTGGGATACATCAACCGTGGAGGAACGTTTTTA
25 CGTTCAGCACGTTATCCTGAATTTGCTGAACCTGAAGGTACGCTTAAAGGGATTGAACAGCTTAAAAA
ACACGGTATTTGAAGGTGTAGTAGTTATCGGTGGTGATGGTCTCTATCATGGTGCTATGCGCTCTAACTG
AGCACGGTTCCTCCAGCTGTGGTTTGCCGGGTACAATTGATAACGATATCGTTGGCACTGACTATACT
ATTGGTTTTGACACAGCAGTTGCGACAGCAGTTGAGAATCTTGACCCGCTCTCGTGATACATCAGCAAG
TCTAATCCGTACTTTTGTGTGTAGGTTATGGGAAGAAATGCAGGAGATATCGCTCTTTGGTCAGGTA
30 TCGCTGAGGTGCAGATCAAAATTTATGTTCTGAAGAAGAGTTCAATATTTGATGAAGTTGTCTCAAAAT
GTATAGAGCTGGCTATGCAGCTGGTAAACATCACCAAATCATCGTCTTCGACAGAGGTGTTATGAGTGG
TGATGAGTTTGC AAAACAATGAAGCAGCAGGAGACGATAGCGATCTTCGTGTGACGAATTTAGGAC
ATCTGCTCCGTGGTGGTAGTCCGACGGCTCGTGATCGTGTCTTAGCATCTCGTATGGGAGCGTACGCT
GTTCAAATTTGTTGAAAGAAGGTCTGGTGGTTTAGCCGTTGGTGTCCACAACGAAGAATGGTTGAAAG
35 TCCAAATTTAGGTTTAGCAGAGAAGAGGTGCTTTGTTACGCTTGACTGATGAAGGAAAAATCGTTGTTA
ATAATCCGCATAAAGCGGACCTTCGCTTGCAGCAGCTTAATCGTGACCTTGCCAACCAAGTAGTAA

SEQ ID NO. 79

MKRIAVLTSGGDAPGMNAAIRAVVRKAISEGMEVYGINQGYGMVIGDIFPLDANSVGDITNRGGTFL
RSARYPEFAELBGQKLGTEQKKKHGIEGVVIVGGDSYHGAMRLTEHGFPAVGLPGTIDNDIVGTDTY
40 IGFDTAVATAVENLDRLRDTSASHNRTFVVVEVMGRNAGDIALWSGIAAGAQIIVPEEEFNIDEVVS
VRAGYAAKGHHQIIVLAEGVMSGDEFKAKTMAAGDDSLRVNLGHLRGGSPPTARDVLASRMGAYA
VQLLEKRGGLAVGVHNEEMVESPIGLAEERALFSLTDEGKIVVNNPHKADRLRLAALNRDLANQSSK

GBS 328

GBS 328 belongs to the 5'-nucleotidase family. Nucleotide and amino acid sequences of GBS 328 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 6015 and SEQ ID 6016. These sequences are set forth below as SEQ ID NOS 80 and 81:

SEQ ID NO. 80

ATGAAAAAGAAATTATTTTGAAGTAGTGTCTTGGTTTAGTCGCTGGGACTTCTATTATGTTCTC
AAGCGTGTTCGCGGACCAAGTCGGTGTCCAAGTTATAGGCGTCAATGACTTTTCATGGTGCACCTTGACA
10 ATACTGGAACAGCAAAATATGCCTGATGGAAAAGTTGCTAATGCTGGTACTGCTGCTCAATTAGATGCT
TATATGGATGACGCTCAAAAAGATTTCAAACAACTAACCCCTAATGGTGAAGCATTAGGGTTCAAGC
AGCGGATATGGTTGGAGCAAGTCCAGCCAACTCTGGGCTTCTTCAAGATGAACCAACTGTGTCAAAATTT
TTAATGCAATGAATGTTGGAGTAGTGGCACTTGGGTACCATGAATTTGATGAAGGGTTGGCAGAAATAT
AATCGTATCGTTACTGGTAAAGCCCCCTGCTCCAGATTCTAATATTAAATAATATTACGAAATCATACCC
15 ACATGAAGCTGCAAAACAGAAATTTGATAGTGGCAAAATGTTATTGATAAAGTTAAACAAACAAATTCCTT
ACAATTTGGAAGCCTTACGCTATTAAAAATATTCCTGTAAATAACAAAAGTGTGAACGTTGGCTTTATC
GGGATTGTGCACAAAGACATCCCAACCTTGTCTTACGTAAAAATTTATGAACAAATATGAATTTTTCAGA
TGAAGCTGAAACATCGTTAAATACGCCAAAGAAATTACAAGCTAAAAATGTCAAAGCTATTGTTAGTTTC
TCGCACATGTACCTGCACCAAGTAAAAATGATATTGCTGAAGGTGAAGCAGCAGAAATGATGAAAAAA
20 GTCAATCAACTCTTCCCTGAAAAATAGCGTAGATATTGCTCTTTGCTGGACACAATCATCAATATACAAA
TGGTCTTTGTTGTAAGTCTGATTGTACAAAGCGCTCTCTCAAGGAAAAGCCATGCTGATGTACGTG
GTGCTTAGATACTGATACACAAGATTTTCATGTAGACCCCTTCAGCTAAAGTAATTCAGTGTGCTCCT
GGTAAAAAAACAGGTAGTGGCGGATATTCAAGCCATTGTTGACCAAGCTAATCTACTTCGTTAAACAACT
25 AACAAGCTAAAAATTTGGTATGCTGCCAGGTAAAGTGTCTATGATACGCTTCTGTTGATCAAGATAATG
TTAGTCCGGTAGGCAAGCTCATCACAGAGGCTCACTAGCAATTTGCTGAAAAAGCTGGCCAGATATC
GATTTTGGCATGACAAATAATGGTGGCATTCTGCTGACTTACTCATCAACCCAGATGGAACAATCAC
CTGGGGAGCTGCACAAGCAGTTCAACCTTTTGGTAATATCTTACAAGTCGTGGAATTTACTGGTAGAG
ATCTTTTATAAAGCATCTCAACGAACAATACGACCAAAAAACAAATTTCTTCTTCAAATAGCTGGTCTG
CGATACACTTACACAGATAAATAAAGAGGGCGGGGAAGAAACACCAATTTTAAAGTTGTAAGAGCTTATAA
30 ATCAAATGGTGAGGAATCAATCCTGATGCAAATACAAATTAAGTTATCAATGACTTTTTATTTCGGTG
TGGTGATGGCTTTGCAAGCTTCAGAAATGCCAACTTCTAGGAGCCATTAAACCCGATACAGAGGTA
TTTATGGCCCTATATCACTGATTTAGAAAAAGCTGGTAAAAAGTGAAGCTTCCAAATAATAAACCTTAA
AATCTATGTCACATGAGATGGTTAATGAACTATTACACAAATGATGGTGCATACATAGCATATTATTA
AGAACTTTATTTAGATGACGAAGGAATTTGTAGCACAAAGAAATTTGATCAGACATCTTAAACCAA
35 ACAAATCAAATCTACAAAAATCAACCCCTGTAACCTCAATTCACAAAAACAATTAACCAATTTTAC
AGCTATTAAACCTATGAGAAATTTATGGCAAAACCATCAACTCCACTACTGTPAATATCAAAACAATTA
CAAAACAAACTCTGAAATATGGACAATCATTCCTTATGCTGTCTTGGTGTGGACCTATAGGAATTT
GCTTTAAATACAAGAAAAACATATGAAA

SEQ ID NO. 81

MKKKIILKSSVGLVAGTSMFSSVFADQVGVQVIGVNDHFHGLDNTGTANMPDGKVANAGTAAQLDA
YMDAQKDFKQTNPNGESIRVQAGDMVGASPNLSGLLQDEPTVKNPNMNVYGTGLGNHFEDEGLAEY
NRIVTGKAPAPDSNNINIKSYSPHEAAKQBIIVVANVIDKVNKQIPYNWKPYAIAKINPVNNKSVNVGFI
GIVTKDIPNLVLRKNYEQYEFDEAETIVKYAKELQAKNVKAIIVLAHVPAATSKNDIAEGGAAEMMKK
45 VNQLFPENSVDIVFAGHNHQVTNGLVGKTRIVQALSQGKAYADVRGVLDTQDFIETPSAKVIAVAP
GKKTGSADIQAIVDQANTIVQVTEAKIGTAEVSMITRSVDQDNVSPVGLITEAQLAIARKSWPDI
DFAMTNNIGIRADLLIKPDGTTIWGAQAQVQFCNIIQVVEITGRDLYKALNEQYDQKQNFLLQIAGL
RYTYTDNKEGGEETPFKVVKAYKSNGBEINPDAKYKLVINDFLFGGGGDFASFRNAKLGLGAINPDET
FMAYITDLEKAGKVKVSPNNPKPIVYTMKVMNETITQNDGTHSIKKLYLDRQGNIVAQEIVSDTLNQ
50 TSKSTKINPVITTHKKQLHQFTAINPMRNYKFPNSNTTVKSKQLPKTNSYEQSFLMSVFGVGLIGI
ALNTKKKHKM

GBS 328 may contain an N-terminal leader or signal sequence region which is indicated by the underlined sequence at the beginning of SEQ ID NO: 81 above. In one embodiment, one or more amino acids from the leader or signal sequence region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 82.

SEQ ID NO: 82

HGALDNTGTANMPDGKVKANAGTAAQLDAYMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDE
PTVKNFNAMNVEYGTGLNHEFDEGLAEYNRIVTGKAPAPDSNINNI TKSYPHEAAKQEI VVANVIDKV
NKQI PYNWKP YAIKNI PVNNKSVNVGFIGIVTKDIPNLVLRKNYEQYEFLEDEAETIVKYAKELQAKNV
KAI VVLAHV PATSKNDIAEGEAAEMMKVNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKA
YADVRGVLDTDTQDFIETPSAKVIAVAPGKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRS
VDQDNVSPVGLSITEAQLAIARKSWPDI DFAMTNNGGIRADLLIKPDGTITWGAAQAVQFPFGNQLQVV
EITGRDLYKALNEQYDQKQNFLLQIAGLRITYTDNKEGGEETPFKVVKAYKSNGEEINPDAKYKLVIN
DLSFGGGDGFASFRNAKLLGAINPDTEVFMAIYITDLEKAGKKVSPNNKPKIYVTMKNVNETITQNDG
THSIIKKLYLDRQGNIVAQEIVSDTLNQTKSKSTKINPVTTIHKQLHQFTAINPMRNYGKPSNSTTV
KSKQLPKTNSYEGQSFLMSVFGVLGIALNTKKHKMK

GBS 328 may also contain a transmembrane and/or cytoplasmic domain region. In one embodiment, one or more amino acids from the transmembrane and/or cytoplasmic domain region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 83.

SEQ ID NO: 83

HKKKIILKSSSVLGLVAGTSMFSSVFADQVGVQVIGVNDHFHALDNTGTANMPDGKVKANAGTAAQLDA
YMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDEPTVKNFNAMNVEYGTGLNHEFDEGLAEY
NRIVTGKAPAPDSNINNI TKSYPHEAAKQEI VVANVIDKVNKQI PYNWKP YAIKNI PVNNKSVNVGFIGI
VIVTKDIPNLVLRKNYEQYEFLEDEAETIVKYAKELQAKNVKAI VVLAHV PATSKNDIAEGEAAEMMK
VNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKAYADVRGVLDTDTQDFIETPSAKVIAVAP
GKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRSVDQDNVSPVGLSITEAQLAIARKSWPDI
DFAMTNNGGIRADLLIKPDGTITWGAAQAVQFPFGNQLQVVEITGRDLYKALNEQYDQKQNFLLQIAGL
RITYTDNKEGGEETPFKVVKAYKSNGEEINPDAKYKLVINDLFGGGDGFASFRNAKLLGAINPDTEVF
MAIYITDLEKAGKKVSPNNKPKIYVTMKNVNETITQNDGTHSIIKKLYLDRQGNIVAQEIVSDTLNQ
TKSKSTKINPVTTIHKQLHQFTAINPMRNYGKPSNSTTVKS

In one embodiment, one or more amino acids from the leader or signal sequence region and one or more amino acids from the transmembrane or cytoplasmic region of GBS 328 are removed. An example of such a GBS 328 fragment is set forth below as SEQ ID NO: 84.

SEQ ID NO: 84

HGALDNTGTANMPDGKVKANAGTAAQLDAYMDDAQKDFKQTNPNGESIRVQAGDMVGASPANSGLLQDE
PTVKNFNAMNVEYGTGLNHEFDEGLAEYNRIVTGKAPAPDSNINNI TKSYPHEAAKQEI VVANVIDKV
NKQI PYNWKP YAIKNI PVNNKSVNVGFIGIVTKDIPNLVLRKNYEQYEFLEDEAETIVKYAKELQAKNV
KAI VVLAHV PATSKNDIAEGEAAEMMKVNQLFPENSVDIVFAGHNHQYTNGLVGKTRIVQALSQGKA
YADVRGVLDTDTQDFIETPSAKVIAVAPGKKTGSADIQAIVDQANTIVKQVTEAKIGTAEVSVMITRS
VDQDNVSPVGLSITEAQLAIARKSWPDI DFAMTNNGGIRADLLIKPDGTITWGAAQAVQFPFGNQLQVV

EITGRDLYKALNEQYDQKQNFLLQIAGLRYTYTDNKEGGEETPFKVVKAYKSNGBEINPDACYKLVIN
DFLFGGGDGEFASFRNAKLGAINEPDTEVFMAIYITDLEKAGKKVSPNNPKPIYVTMKMVNETITQNDG
THSIIKKLYLDRQGNIVAQEIVSDTLNQTTSKSTKINPVTTTHKKQLHQETAINPMRNYGKPSNSTTV
KS

GBS 656

GBS 656 refers to a putative DNA-entry nuclease. Nucleotide and amino acid sequences of GBS 656 sequenced from serotype V isolated strain 2603 V/R are set forth in Ref. 2 as SEQ ID 9323 and SEQ ID 9324. These sequences are set forth below as SEQ ID NOS 85 and 86:

SEQ ID NO. 85

ATGAAAAGATTACATAAACTGTTTATAACCGTAATTGCTACATTAGGTATGTTGGGGGTAATGACCTT
TGGTCTTCCACGCGAGCCGCAAAACGTAAACGCCGATAGTACATGCTGATGTCAATTATCATCTGTTGATA
CGAGCCAGGAATTTCAAATAATTTAAAAAATGCTATTGGTAACCTACCATTTCATATGTTAATGGT
ATTTATGAATTAATAATAATATCAGACAAATTTAAATGCTGATGTCAATGTTAAAGCGTATGTTCAAAA
TACAATTGCAATCAACAAAGACTATCAACTGCTAATGCAATGCTTGATAGAACATTGCTCAATATC
AAAATCGCAGAGATACCACTCTCCCGATGCAAAATGGAAACCAATTAGTTGGCATCAAGTAGCTACT
AATGACCAATTATGGACATGCAGTCGACGACAGGGGCATTTAATTGCCTATGCTTAGCTGGAAATTTCAA
AGGTTGGGATGCTTCCGTGTCAAAATCCTCAAAATGTTGTACACAAACAGCTCATTTCAACCAATCAA
ATCAAAAATCAATCGTGGACAAATTTATATGAAAGCTTAGTTTCGTAAGGCGGTTGACCAAAACAAA
CGTGTTCTGTACCGTGTAACCTCCATTGTACCGTAATGATGACTGATTAGTTCATTTGCAATGCACT
AGAAGCTAAATCACAAGATGGCACCATTAGAATTTAATGTTGCTATTCCAAACACACAAGCATCATACA
CTATGATTATGCAACAGGAGAAATAACACTAAAT

SEQ ID NO. 86

MKRLHKLFIITVIALTGLMLGVMTEFGLTPQPNVPIVHADVNSSVDTSQEFQNNLKNAINLFPQYVNG
IYELNNNTQLNADVNKAYVQNTIDNQQLSTANAMLDRTIRQYQNRRTTLPDANWKPLGHWQVAT
NDHYHGAVDKGLHIALYALAGNFKGWDASVSNPQNVVTQTAHSNQSNGKINRGQNYYESILVRKAVDQNK
RVRVRYVTFPLRNDDLVFPMHLEAKSQDGTLEFNVAIPNTQASVYTM DYATGEITIN

GBS 67

The following offers examples of preferred GBS 67 fragments. Nucleotide and amino acid sequence of GBS 67 sequences from serotypeV isolated strain 2603 are set forth below as SEQ ID NOS: 87 and 88.

SEQ ID NO. 87

ATGAGAAAATACCAAAAATTTCTAAAATATTGACGTTAAGTCTTTTTGTTGTGCGCAAAATACCGCT
TAA TACCAATGTTT TAGGGGAAAGTACCGTACCGGAAAATGGTGCTAAGGAAAGTTAGTTGTTAAAA
AGA CAGATGACCGAGAACAACCACTTTCAAAGCTACCTTTGTTTAAAACTACTGCTCATCCAGAA
AGT AAAATAGAAAAGTAATGCTGAGCTTAACAGGTGAAGCTACTTTTGATAATCTCATACCTGGAGA
TTA TACTTTATCAGAAGAAACAGCGCCCGAAGGTATAAAAAGACTAACCAGACTTGGCAAGTTAAGG
TTGAGAGTAATGGAAAACTACGATACAAAAATAGTGGTGATAAAAATTCACAAATGGACAAAAATCAG
GAA GAAC TAGTAAGCAGTATCCCCCAGGAAATTTATGAAGATACAAAGGAATCTTATAAACTTGA
GCA GTTTAAAGGTTTCAGTTCCAAATGGAAAGTCAGAGGCAAAAGCACTTAACCAATATTCAAGTGAAG
GTGAGCATATAAGAGAAATTCAGAGGGAACATTATCTAAACGTATTTTCAAGTAGGTGATTATGACT
CAT AATAAATATAAAATTTGAGTTAACTGTGCTGGAAAAACCATAGTAAACCAAGTGGACAAACAAAA
GCC GTTAGACTGTTGCTCTCTGCTACTCGATAATTCTAATCAATGAATAACAGTGGCCCAAAATTTTCAAA
GGCATAATAAAGCCAAAGAAAGCTGCCGAAGCTCTGGGACCGCAGTAAAGATATTTTAGGAGCAAC

AGTGATAATAGGGTTGCATTAGTTACCTATGGTTTCAGATATTTTTGATGGTAGGAGTGTAGATGTCGT
 AAAAGGATTTTAAAGAGATGATAAATATTATGGCCTTCAAACCTAAGTTCCACAATTCAGACAGAGAATT
 ATAGTCATAAACAATTAACAAATAATGCTGAAGAGATTATAAAAAGGATTCGCACAGAGCTCCATAAA
 GCTAAGTGGGGATCTACTACCAATGGATTAACTCCAGAGCAACAAAAGGAGTACTATCTTAGTAAAGT
 5 AGGAGAAACATTTACTATGAAAGCCTTCATGGAGGCAGATGATATTTGAGTCAAGTAAATCGAAATA
 GTCAAAAATATTATTGCTACTGTAACCTGATGGTGTCTTACGAGATCATATGCTATTATAAATTTTAA
 CTGGGTGCATCATATGAAGGCCAATTTGAACAAATGAAAAAATGGATATCTAATAAAGTAATTT
 TCTACTTACTGATTAAGCCCGAGGATATAAAGGAATGGGAGAGTTAC'TTTTGT'TTCCCTTAGATA
 GTTATCAACACACAGATAATCTTGGAAACTTACAAAACTTCATTATTTAGATTAAATCTTAATCTTAC
 10 CCTAAGGTACAATTTATCGAAATGGACAGTGAAGAACATGGAAACCAACCAACCTTTATATAAA
 TAGTTTAAACAGAAAAATATGACATTTTAAATTTTGGTATCGATAATCTGTTT'TAGACAAGTTT
 ATAATTGAGGAGTATAAGAAAAATCAAGATGGTACTTTTCAAAAATGAAAGAGGAAGCTTTTAAACTT
 TCAGATGGAGAAATCAGAACTAATGAGGTGTTCTCTTCCAAACCTGAGTACTACACCCCTATCGT
 AACTTCAGCCCATACATCTAACATGAAATTTTATCTAAAATTCAGCAACAATTTGAAACCTTTTAA
 15 CAAAAGAAACTCAATTTGTTAATGGAACATCGAAGATCCTATGGGTGATAAAATCAATTTACAGCTT
 GGTAAATGGACAAACATTACAGCCAAAGTATTATCTTTACAGGGAAATGATGGAAGTGAATGAAGGA
 TGGTATTGCAACTGGTGGGCTTAATATGATGGTGAATCTTAAGGGGGTTAAATGAGAATACATCG
 GAAATAAATCTTATGTTAGAGGTTGAATTTAGGAGAAGGTCAAAAAGTAACACTACATATGATGTG
 AAACTAGATGAGCTTTTATAAGATAACAAATCTATGACACTAATGGTAGAACCAACTGAATCTGATA
 20 GTCAGAGGATCCTAATACACTTAGAGATTTTCCAATCCCTAAAATTCGTGATGTGAGAGAATATCCTA
 CAATAACGATTAAAAACGAGAAGGATTAGGTGAAATTTGAATTTATAAAAAGTTGATAAAGATAATAAT
 AAGTTGCTTTCAAAAGGAGCTACGTTTGAACCTCAAGAAATTTAATGAGATTATTAACCTTTATTACC
 AATAAAAATAATTAATCAAAAGTAGTGACGGGAGAAAACGGCAAAATTTCTTACAAGAGATTGAAAG
 ATGCAAAATATCAGTTAATGAAGCAGTTTTCGCCGGAGGATTATCAAAAATTTACTAATAAACCAAT
 25 TTAACCTTTGAAAGTGTATAAGGATCGATAAAAATATAATAGCTGTAAATAACAGATTTCTGAAATA
 TCAATGAGGAAGGTGACAGCAATTAATACCAACACGCAATATCCACAAAAGGAATATTCCCTATGA
 CAGGTGGGAAGGAATTCATCTTTTCAATTTAATAGGTGGAGCTATGATGCTCTATTGACAGTGAAT
 TATAATTGGAAGGATATAAGAACTTAGTGATATGTCATCAAAAAGAT

SEQ ID NO: 88

MRKYQKFSKILTLSLFCLSQIPLNTNVLGESTVPENGAKGLVVKKTDQNKFLSKATFVLTKTTHAFPE
 SKIEVTAELTGEATFDNLIPGDYTLSEETAPEGYKKTNQTWQVKVBSNGKTTIQNSGDKNSTTGQNQ
 EELDKQYPPGTGIYEDTKESYKLEHVKGSPVNGKSEAKAVNPYSSEGEHIREIPEGTLKSRISEVGDLA
 HNKYKIELTVSGKTIIVKPVOKQKPLDVVFLDNSNSMNDGPNFQRHNKAKKAAEALGTAVKDILGAN
 35 SDNRVALVTYGSDFIDGRSVDVVGKFKEDDKYGLQTKFTITQENYSHKQLTNAAEIIKRIPTAEAPK
 AKWGSTTNGLTPEQKQKEYLSSKVGETFTMKAFMEADDILSQVNRNSKIIIVHTDGVPTRSYAINNPK
 LGASYESQFEQMKHGYLNKSNFLLTDKPEDIKSGNGESYFLPFLDSYQTQIISGNLQKLHYLDLNLNY
 PKGTIYRNGPVKEHGTPTKLYIINSLKQKNYDIFNPGDISGFRQVYNEEYKKNQDGTQRLKEBAFLK
 SDGEITELMRFSFSSKPEYPTPIVTSADTSNNELSKIQQQPETILLKENSIVNGTIEDPMGDKNLQL
 40 GNGQTLQPSDYTLQGNDSVPMKDIATGGFNNDGGILKGVLKEYIGKNLVRELNNGEQKVTLLTYDV
 KLDDSFISNKPYDTNNGRTTLNPKSEDPNTLRDFPIPKIRDBVREYPTTIIRNEKKLGEIEFIKVKDKDNN
 KLLLKGAATFELQEFNEDYKLYLPKNNNSKVVTGENGKISYKLDKDGKYLIEAVSPEDYQKINTKPI
 LTFEVVKSIKNIIAVKNQKISEYHEBGDKHLINTHIPPKEGIIPMTGGKILSFILIGGAMSTAGGI
 45 YIWKRYKKSSDMSIKKD

GBS 67 contains a C-terminus transmembrane region which is indicated by the underlined region closest to the C-terminus of SEQ ID NO: 88 above. In one embodiment, one or more amino acids from the transmembrane region is removed and/or the amino acid is truncated before the transmembrane region. An example of such a GBS 67 fragment is set forth below as SEQ ID NO: 89.

SEQ ID NO: 89

MRKYQKFSKILTL~~SLFCL~~SIPLNTNVLGESTVPENGAKGKLVVKKTTDDQNKPLSKATFVLKTTAHPE
 SKIEKVTAELTGEATFDNLI~~PGDYTL~~SEETAPEGYKKTNTQTQVKVNESNGKTTIQNSGDKNSTIGQNQ
 EELDKQYPTTGIYEDTKESYKLEHVKGSPVNGKSEAKAVNPYSSBGEHIREIPEGLTSKRISVEVGDLA
 HNKYKIELTVSGKTI~~VKVPDKQKPLD~~VVFLD~~NSNSM~~NDGNPFRHNKAKKAAEALGTAVKDILGAN
 SDNRVALVTYGS~~DI~~FDGRSV~~DV~~VKGFKEDDKYGLQTKFTIQTENYSHKQLTNNAAEIIKRIPT~~EAPK~~
 AKWGSTTNGLTPEQQKEYYLSKVGETFTMKA~~FMEADDILS~~QVNRNSQKIIVHVT~~DGVP~~TRSYAINNFK
 LGASY~~BSQ~~FEQMKKNGYLNKSNFLLTDKPB~~DI~~KNGESYFLFPLDSYQTQIISGNLQK~~LHYD~~LNLNY
 PKGTIYRNGPVKEHGTPTKLYINSLKQKNYDIFNFGIDISGRQVYNEEYKKNQDGTFOKLKEEAFKL
 SDGEITELMRSFSSKPEY~~YTP~~IVTSADTSNNEILSKIQQQFETILT~~KENS~~IVNGTIEDPMGD~~KINL~~QL
 GNGQTLQPSDYTLQGN~~DG~~SVMKDGIATGGPNNDGGILKGVKLEYIGNKLYVRGLNLGEGQKVTLTYDV
 KLDDSPISNKFYDTNGRTTLNPKSEDNTLRDFFIPKIRDVREYPTITIKNEKKLGIEIFIKVDKDN
 KLLLKGA~~T~~FPLEQFNE~~DY~~KLYLP~~IK~~NNNSKVVTGENGKISYKDLKDGKYQLIEAVSPEDYQKITNKPI
 LTFEVVGKSIKNI~~IAV~~NKQISEYHEEGDKHLITNTHIPP~~KGI~~MPMTGGKGLS

GBS 67 contains an amino acid motif indicative of a cell wall anchor (an LPXTG motif):

SEQ ID NO: 90 *IPMTG*. (shown in *italics* in SEQ ID NO: 88 above). In some recombinant host cell systems, it may be preferable to remove this motif to facilitate secretion of a recombinant GBS 67 protein from the host cell. Accordingly, in one preferred fragment of GBS 67 for use in the invention, the transmembrane and the cell wall anchor motif are removed from GBS 67. An example of such a GBS 67 fragment is set forth below as SEQ ID NO: 91.

SEQ ID NO: 91

MRKYQKFSKILTL~~SLFCL~~SIPLNTNVLGESTVPENGAKGKLVVKKTTDDQNKPLSKATFVLKTTAHPE
 SKIEKVTAELTGEATFDNLI~~PGDYTL~~SEETAPEGYKKTNTQTQVKVNESNGKTTIQNSGDKNSTIGQNQ
 EELDKQYPTTGIYEDTKESYKLEHVKGSPVNGKSEAKAVNPYSSBGEHIREIPEGLTSKRISVEVGDLA
 HNKYKIELTVSGKTI~~VKVPDKQKPLD~~VVFLD~~NSNSM~~NDGNPFRHNKAKKAAEALGTAVKDILGAN
 SDNRVALVTYGS~~DI~~FDGRSV~~DV~~VKGFKEDDKYGLQTKFTIQTENYSHKQLTNNAAEIIKRIPT~~EAPK~~
 AKWGSTTNGLTPEQQKEYYLSKVGETFTMKA~~FMEADDILS~~QVNRNSQKIIVHVT~~DGVP~~TRSYAINNFK
 LGASY~~BSQ~~FEQMKKNGYLNKSNFLLTDKPB~~DI~~KNGESYFLFPLDSYQTQIISGNLQK~~LHYD~~LNLNY
 PKGTIYRNGPVKEHGTPTKLYINSLKQKNYDIFNFGIDISGRQVYNEEYKKNQDGTFOKLKEEAFKL
 SDGEITELMRSFSSKPEY~~YTP~~IVTSADTSNNEILSKIQQQFETILT~~KENS~~IVNGTIEDPMGD~~KINL~~QL
 GNGQTLQPSDYTLQGN~~DG~~SVMKDGIATGGPNNDGGILKGVKLEYIGNKLYVRGLNLGEGQKVTLTYDV
 KLDDSPISNKFYDTNGRTTLNPKSEDNTLRDFFIPKIRDVREYPTITIKNEKKLGIEIFIKVDKDN
 KLLLKGA~~T~~FPLEQFNE~~DY~~KLYLP~~IK~~NNNSKVVTGENGKISYKDLKDGKYQLIEAVSPEDYQKITNKPI
 LTFEVVGKSIKNI~~IAV~~NKQISEYHEEGDKHLITNTHIPP~~KGI~~

The compositions of the invention may also include combinations including one or more known GBS antigens in combination with GBS 80.

There is an upper limit to the number of GBS antigens which will be in the compositions of the invention. Preferably, the number of GBS antigens in a composition of the invention is less than 20, less than 19, less than 18, less than 17, less than 16, less than 15, less than 14, less than 13, less than 12, less than 11, less than 10, less than 9, less than 8, less than 7, less than 6, less than 5, less than 4, or less than 3. Still more preferably, the number of GBS antigens in a composition of the invention

is less than 6, less than 5, or less than 4. Still more preferably, the number of GBS antigens in a composition of the invention is 3.

The GBS antigens used in the invention are preferably isolated, i.e., separate and discrete, from the whole organism with which the molecule is found in nature or, when the polynucleotide or polypeptide is not found in nature, is sufficiently free of other biological macromolecules so that the polynucleotide or polypeptide can be used for its intended purpose.

Fusion Proteins

The GBS antigens used in the invention may be present in the composition as individual separate polypeptides, but it is preferred that at least two (i.e. 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18) of the antigens are expressed as a single polypeptide chain (a "hybrid" or "fusion" polypeptide). Such fusion polypeptides offer two principal advantages: first, a polypeptide that may be unstable or poorly expressed on its own can be assisted by adding a suitable fusion partner that overcomes the problem; second, commercial manufacture is simplified as only one expression and purification need be employed in order to produce two polypeptides which are both antigenically useful.

The fusion polypeptide may comprise two or more polypeptide sequences from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690 and GBS 691. Preferably, the polypeptide sequences are selected from the group consisting of GBS 80, GBS 104 and GBS 322. Most preferably, the fusion peptide includes a polypeptide sequence from GBS 80. Accordingly, the invention includes a fusion peptide comprising a first amino acid sequence and a second amino acid sequence, wherein said first and second amino acid sequences are selected from a GBS antigen or a fragment thereof of the above antigen group. Preferably, the first and second amino acid sequences in the fusion polypeptide comprise different epitopes.

EXAMPLE 7: Examples of fragments for fusion proteins from GBS 80 with GBS 104, and GBS 322

Examples of GBS fragments for fusion proteins are provided from GBS 322, GBS 104, and GBS 80. One example of a fragment of GBS 322 in a fusion protein is a 407 amino acid fragment with the signal peptide removed. Fragments of GBS 104 may also be incorporated in fusion proteins. An example of GBS 104 fragments includes an 830 amino acid fragment, a 359 amino acid fragment from near the N-terminus, a 581 amino acid fragment from near the N-terminus, and a 740 amino acid fragment from near the N-terminus. Examples of GBS 80 fragments include a 446 amino acid fragment and a 235 amino acid fragment. Table 13 below summarizes the examples of fragments for fusion proteins and their locations within the corresponding full length GBS protein.

Table 13: Active Maternal Immunization Assay using combinations of GBS 80 with GBS 104 and GBS 322

GBS	Size (AA)	SEQ ID NO	From ... to
322	407	92	25-432
104	830	96	28-858
104 N1	359	97	28-387
104 N2	581	98	28-609
104 N3	740	99	28-768
80	446	100	37-483
80N	235	101	37-272

5

Hybrids (or fusions) consisting of amino acid sequences from two, three, four, five, six, seven, eight, nine, or ten GBS antigens are preferred. In particular, hybrids consisting of amino acid sequences from two, three, four, or five GBS antigens are preferred.

10 Different hybrid polypeptides may be mixed together in a single formulation. Within such combinations, a GBS antigen may be present in more than one hybrid polypeptide and/or as a non-hybrid polypeptide. It is preferred, however, that an antigen is present either as a hybrid or as a non-hybrid, but not as both.

Hybrid polypeptides can be represented by the formula $\text{NH}_2\text{-A-}\{-\text{X-L}\}_n\text{-B-COOH}$, wherein:
 15 X is an amino acid sequence of a GBS antigen or a fragment thereof from the antigen group set forth above; L is an optional linker amino acid sequence; A is an optional N-terminal amino acid sequence; B is an optional C-terminal amino acid sequence; and n is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15.

If a -X- moiety has a leader peptide sequence in its wild-type form, this may be included or omitted in the hybrid protein. In some embodiments, the leader peptides will be deleted except for that of the -X- moiety located at the N-terminus of the hybrid protein *i.e.* the leader peptide of X_1 will
 20 be retained, but the leader peptides of $\text{X}_2 \dots \text{X}_n$ will be omitted. This is equivalent to deleting all leader peptides and using the leader peptide of X_1 as moiety -A-.

For each n instances of $\{-\text{X-L}\}$, linker amino acid sequence -L- may be present or absent. For instance, when $n=2$ the hybrid may be $\text{NH}_2\text{-X}_1\text{-L}_1\text{-X}_2\text{-L}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-X}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-L}_1\text{-X}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-X}_2\text{-L}_2\text{-COOH}$, *etc.* Linker amino acid sequence(s) -L- will typically
 25 be short (*e.g.* 20 or fewer amino acids *i.e.* 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples comprise short peptide sequences which facilitate cloning, poly-glycine linkers (*i.e.* comprising Gly_n where $n = 2, 3, 4, 5, 6, 7, 8, 9, 10$ or more), and histidine tags (*i.e.* His_n where $n = 3, 4, 5, 6, 7, 8, 9, 10$ or more). Other suitable linker amino acid sequences will be apparent to those skilled in the art. A useful linker is GSGGGG, with the Gly-Ser dipeptide being formed from a

*Bam*HI restriction site, thus aiding cloning and manipulation, and the (Gly)₄ tetrapeptide being a typical poly-glycine linker.

-A- is an optional N-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include leader sequences to direct protein trafficking, or short peptide sequences which facilitate cloning or purification (*e.g.* histidine tags *i.e.* His_n where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more). Other suitable N-terminal amino acid sequences will be apparent to those skilled in the art. If X₁ lacks its own N-terminus methionine, -A- is preferably an oligopeptide (*e.g.* with 1, 2, 3, 4, 5, 6, 7 or 8 amino acids) which provides a N-terminus methionine.

-B- is an optional C-terminal amino acid sequence. This will typically be short (*e.g.* 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include sequences to direct protein trafficking, short peptide sequences which facilitate cloning or purification (*e.g.* comprising histidine tags *i.e.* His_n where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more), or sequences which enhance protein stability. Other suitable C-terminal amino acid sequences will be apparent to those skilled in the art. Most preferably, *n* is 2 or 3.

**EXAMPLE 8: Active Maternal Immunization Assay using fusion proteins of
Fragments of GBS 80, GBS 67, and GBS 322**

In this example, fusion proteins of GBS antigens was used in the Active Maternal Immunization Assay with an isolate challenge of different GBS strains. In these experiments, the challenge dose for the different GBS strains was sufficient to kill approximately 70 – 90% of unimmunized pups and is equal to 10 x LD 50% (where LD 50% is the statistically derived Median Lethal Dose). The maternal mice were immunized according to the Active Maternal Immunization Assay schedule described above with the fusion proteins of a GBS 80 antigen with GBS 322 antigen in the GBS strains set forth in Table 14 below. Survival % was observed with the GBS fusion proteins. As shown in Table 14, in this particular challenge study, the survival rates for the fusion proteins in all of the GBS strains achieved up to 79%.

Table 14: Active Maternal Immunization Assay using fusion proteins of GBS 80 with GBS 322

	COH1 (III)		CJB111 (V)		515 (Ia)		DK21 (II)		2603 (V)	
GBS	Dead/ treated	Survival %	Dead/ treated	Survival %	Dead/ treated	Survival %	Dead/ treated	Survival %	Dead/ treated	Survival %
80N-322	16/40	60	8/39	79	12/28	57	7/19	63	8/37	78
80	4/24	83								
PBS	35/40	12	27/35	23	32/39	18	31/40	22	33/40	17
80-322	12/27	55							12/38	68
80	0/33	100	28/40	30						
322									1/16	94
PBS	19/20	5	38/39	2	25/29	14			19/26	27

Nucleic Acids

The invention also provides nucleic acid encoding the GBS antigens and/or the hybrid fusion polypeptides of the invention. Furthermore, the invention provides nucleic acid which can hybridise to these nucleic acids, preferably under "high stringency" conditions (*e.g.* 65°C in a 0.1xSSC, 0.5% SDS solution).

Polypeptides of the invention can be prepared by various means (*e.g.* recombinant expression, purification from cell culture, chemical synthesis, *etc.*) and in various forms (*e.g.* native, fusions, non-glycosylated, lipidated, *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other GAS or host cell proteins).

Nucleic acid according to the invention can be prepared in many ways (*e.g.* by chemical synthesis, from genomic or cDNA libraries, from the organism itself, *etc.*) and can take various forms (*e.g.* single stranded, double stranded, vectors, probes, *etc.*). They are preferably prepared in substantially pure form (*i.e.* substantially free from other GBS or host cell nucleic acids).

The term "nucleic acid" includes DNA and RNA, and also their analogues, such as those containing modified backbones (*e.g.* phosphorothioates, *etc.*), and also peptide nucleic acids (PNA), *etc.* The invention includes nucleic acid comprising sequences complementary to those described above (*e.g.* for antisense or probing purposes).

The invention also provides a process for producing a polypeptide of the invention, comprising the step of culturing a host cell transformed with nucleic acid of the invention under conditions which induce polypeptide expression.

The invention provides a process for producing a polypeptide of the invention, comprising the step of synthesising at least part of the polypeptide by chemical means.

The invention provides a process for producing nucleic acid of the invention, comprising the step of amplifying nucleic acid using a primer-based amplification method (e.g. PCR).

- 5 The invention provides a process for producing nucleic acid of the invention, comprising the step of synthesising at least part of the nucleic acid by chemical means.

Purification and Recombinant Expression

- 10 The GBS antigens of the invention may be isolated from *Streptococcus agalactiae*, or they may be recombinantly produced, for instance, in a heterologous host. Preferably, the GBS antigens are prepared using a heterologous host. The heterologous host may be prokaryotic (e.g. a bacterium) or eukaryotic. It is preferably *E.coli*, but other suitable hosts include *Bacillus subtilis*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Neisseria lactamica*, *Neisseria cinerea*, *Mycobacteria* (e.g. *M.tuberculosis*), yeasts, etc.

- 15 Recombinant production of polypeptides is facilitated by adding a tag protein to the GBS antigen to be expressed as a fusion protein comprising the tag protein and the GBS antigen. Such tag proteins can facilitate purification, detection and stability of the expressed protein. Tag proteins suitable for use in the invention include a polyarginine tag (Arg-tag), polyhistidine tag (His-tag), FLAG-tag, Strep-tag, c-myc-tag, S-tag, calmodulin-binding peptide, cellulose-binding domain, SBP-
20 tag,, chitin-binding domain, glutathione S-transferase-tag (GST), maltose-binding protein, transcription termination anti-terminiation factor (NusA), *E. coli* thioredoxin (TrxA) and protein disulfide isomerase I (DsbA). Preferred tag proteins include His-tag and GST. A full discussion on the use of tag proteins can be found at Ref. 3.

- 25 After purification, the tag proteins may optionally be removed from the expressed fusion protein, i.e., by specifically tailored enzymatic treatments known in the art. Commonly used proteases include enterokinase, tobacco etch virus (TEV), thrombin, and factor X_a.

GBS polysaccharides

- 30 The compositions of the invention may be further improved by including GBS polysaccharides. Preferably, the GBS antigen and the saccharide each contribute to the immunological response in a recipient. The combination is particularly advantageous where the saccharide and polypeptide provide protection from different GBS serotypes.

- The combined antigens may be present as a simple combination where separate saccharide and polypeptide antigens are administered together, or they may be present as a conjugated
35 combination, where the saccharide and polypeptide antigens are covalently linked to each other.

Thus the invention provides an immunogenic composition comprising (i) one or more GBS polypeptide antigens and (ii) one or more GBS saccharide antigens. The polypeptide and the polysaccharide may advantageously be covalently linked to each other to form a conjugate.

Between them, the combined polypeptide and saccharide antigens preferably cover (or provide protection from) two or more GBS serotypes (e.g. 2, 3, 4, 5, 6, 7, 8 or more serotypes). The serotypes of the polypeptide and saccharide antigens may or may not overlap. For example, the polypeptide might protect against serogroup II or V, while the saccharide protects against either serogroups Ia, Ib, or III. Preferred combinations protect against the following groups of serotypes: (1) serotypes Ia and Ib, (2) serotypes Ia and II, (3) serotypes Ia and III, (4) serotypes Ia and IV, (5) serotypes Ia and V, (6) serotypes Ia and VI, (7) serotypes Ia and VII, (8) serotypes Ia and VIII, (9) serotypes Ib and II, (10) serotypes Ib and III, (11) serotypes Ib and IV, (12) serotypes Ib and V, (13) serotypes Ib and VI, (14) serotypes Ib and VII, (15) serotypes Ib and VIII, (16) serotypes II and III, (17) serotypes II and IV, (18) serotypes II and V, (19) serotypes II and VI, (20) serotypes II and VII, (21) serotypes II and VIII, (22) serotypes III and IV, (23) serotypes III and V, (24) serotypes III and VI, (25) serotypes III and VII, (26) serotypes III and VIII, (27) serotypes IV and V, (28) serotypes IV and VI, (29) serotypes IV and VII, (30) serotypes IV and VIII, (31) serotypes V and VI, (32) serotypes V and VII, (33) serotypes V and VIII, (34) serotypes VI and VII, (35) serotypes VI and VIII, and (36) serotypes VII and VIII.

Still more preferably, the combinations protect against the following groups of serotypes: (1) serotypes Ia and II, (2) serotypes Ia and V, (3) serotypes Ib and II, (4) serotypes Ib and V, (5) serotypes III and II, and (6) serotypes III and V. Most preferably, the combinations protect against serotypes III and V.

Protection against serotypes II and V is preferably provided by polypeptide antigens.

Protection against serotypes Ia, Ib and/or III may be polypeptide or saccharide antigens.

In one embodiment, the immunogenic composition comprises a GBS saccharide antigen and at least two GBS polypeptide antigens or fragments thereof, wherein said GBS saccharide antigen comprises a saccharide selected from GBS serotype Ia, Ib, and III, and wherein said GBS polypeptide antigens comprise a combination of at least two polypeptide or a fragment thereof selected from the antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691. Preferably, the combination includes one or more of GBS 80, GBS 104 and GBS 322. Still more preferably, the combination includes GBS 80 or a fragment thereof.

In certain embodiments, the compositions of the invention do not include a GBS polysaccharide. In certain embodiments, the combination does not include one or more of the GBS antigens selected from the group consisting of GBS 4, GBS 22, GBS 85, GBS 338 and GBS 361.

Immunogenic compositions and medicaments

Compositions of the invention are preferably immunogenic compositions, and are more preferably vaccine compositions. The pH of the composition is preferably between 6 and 8, preferably about 7. The pH may be maintained by the use of a buffer. The composition may be
5 sterile and/or pyrogen-free. The composition may be isotonic with respect to humans.

Vaccines according to the invention may either be prophylactic (*i.e.* to prevent infection) or therapeutic (*i.e.* to treat infection), but will typically be prophylactic. Accordingly, the invention includes a method for the therapeutic or prophylactic treatment of a *Streptococcus agalactiae* infection in an animal susceptible to streptococcal infection comprising administering to said animal a
10 therapeutic or prophylactic amount of the immunogenic compositions of the invention.

The invention also provides a composition of the invention for use as a medicament. The medicament is preferably able to raise an immune response in a mammal (*i.e.* it is an immunogenic composition) and is more preferably a vaccine.

The invention also provides the use of the compositions of the invention in the manufacture of
15 a medicament for raising an immune response in a mammal. The medicament is preferably a vaccine.

The invention also provides for a kit comprising a first component comprising a combination of GBS antigens.

The invention also provides a delivery device pre-filled with the immunogenic compositions of the invention.

The invention also provides a method for raising an immune response in a mammal
20 comprising the step of administering an effective amount of a composition of the invention. The immune response is preferably protective and preferably involves antibodies and/or cell-mediated immunity. The method may raise a booster response.

The mammal is preferably a human. Where the vaccine is for prophylactic use, the human is
25 preferably a female (either of child bearing age or a teenager). Alternatively, the human may be elderly (e.g., over the age of 50, 55, 60, 65, 70 or 75) and may have an underlying disease such as diabetes or cancer. Where the vaccine is for therapeutic use, the human is preferably a pregnant female or an elderly adult.

These uses and methods are preferably for the prevention and/or treatment of a disease caused
30 by *Streptococcus agalactiae*. The compositions may also be effective against other streptococcal bacteria.

One way of checking efficacy of therapeutic treatment involves monitoring GBS infection after administration of the composition of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses against the GBS antigens in the
35 compositions of the invention after administration of the composition.

Compositions of the invention will generally be administered directly to a patient. Direct delivery may be accomplished by parenteral injection (*e.g.* subcutaneously, intraperitoneally, intradermally, intravenously, intramuscularly, or to the interstitial space of a tissue), or by rectal, oral (*e.g.* tablet, spray), vaginal, topical, transdermal (*e.g.* see ref. 4) or transcutaneous (*e.g.* see refs. 5 & 6), intranasal (*e.g.* see ref. 7), ocular, aural, pulmonary or other mucosal administration.

The invention may be used to elicit systemic and/or mucosal immunity.

Dosage treatment can be a single dose schedule or a multiple dose schedule. Multiple doses may be used in a primary immunisation schedule and/or in a booster immunisation schedule. In a multiple dose schedule the various doses may be given by the same or different routes *e.g.* a parenteral prime and mucosal boost, a mucosal prime and parenteral boost, *etc.*

The compositions of the invention may be prepared in various forms. For example, the compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared (*e.g.* a lyophilised composition). The composition may be prepared for topical administration *e.g.* as an ointment, cream or powder. The composition may be prepared for oral administration *e.g.* as a tablet or capsule, as a spray, or as a syrup (optionally flavoured). The composition may be prepared for pulmonary administration *e.g.* as an inhaler, using a fine powder or a spray. The composition may be prepared as a suppository or pessary. The composition may be prepared for nasal, aural or ocular administration *e.g.* as drops. The composition may be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. Such kits may comprise one or more antigens in liquid form and one or more lyophilised antigens.

Immunogenic compositions used as vaccines comprise an immunologically effective amount of antigen(s), as well as any other components, as needed. By 'immunologically effective amount', it is meant that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (*e.g.* non-human primate, primate, *etc.*), the capacity of the individual's immune system to synthesise antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials.

Further Components of the Composition

The composition of the invention will typically, in addition to the components mentioned above, comprise one or more 'pharmaceutically acceptable carriers', which include any carrier that does not itself induce the production of antibodies harmful to the individual receiving the

composition. Suitable carriers are typically large, slowly metabolised macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, and lipid aggregates (such as oil droplets or liposomes). Such carriers are well known to those of ordinary skill in the art. The vaccines may also contain diluents, such as water, saline, glycerol, *etc.* Additionally, auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, may be present. A thorough discussion of pharmaceutically acceptable excipients is available in reference 8.

Vaccines of the invention may be administered in conjunction with other immunoregulatory agents. In particular, compositions will usually include an adjuvant.

Preferred further adjuvants include, but are not limited to, one or more of the following set forth below:

A. Mineral Containing Compositions

Mineral containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminium salts and calcium salts. The invention includes mineral salts such as hydroxides (e.g. oxyhydroxides), phosphates (e.g. hydroxyphosphates, orthophosphates), sulphates, *etc.* {e.g. see chapters 8 & 9 of ref. 9}, or mixtures of different mineral compounds, with the compounds taking any suitable form (e.g. gel, crystalline, amorphous, *etc.*), and with adsorption being preferred. The mineral containing compositions may also be formulated as a particle of metal salt. See ref. 10.

B. Oil-Emulsions

Oil-emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer). See WO90/14837. See also, Frey et al., "Comparison of the safety, tolerability, and immunogenicity of a MF59-adjuvanted influenza vaccine and a non-adjuvanted influenza vaccine in non-elderly adults", Vaccine (2003) 21:4234 – 4237.

Particularly preferred adjuvants for use in the compositions are submicron oil-in-water emulsions. Preferred submicron oil-in-water emulsions for use herein are squalene/water emulsions optionally containing varying amounts of MTP-PE, such as a submicron oil-in-water emulsion containing 4-5% w/v squalene, 0.25-1.0% w/v Tween 80™ (polyoxyethylthylenesorbitan monooleate), and/or 0.25-1.0% Span 85™ (sorbitan trioleate), and, optionally, N-acetyl-muramyl-L-alanyl-D-isoglutamyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3-hydroxyphosphoryloxy)-ethylamine (MTP-PE), for example, the submicron oil-in-water emulsion known as "MF59" (International Publication No. WO 90/14837; U.S. Patent Nos. 6,299,884 and 6,451,325, incorporated herein by reference in their entireties; and Ott et al.,

"MF59 -- Design and Evaluation of a Safe and Potent Adjuvant for Human Vaccines" in *Vaccine Design: The Subunit and Adjuvant Approach* (Powell, M.F. and Newman, M.J. eds.) Plenum Press, New York, 1995, pp. 277-296). MF59 contains 4-5% w/v Squalene (e.g., 4.3%), 0.25-

0.5% w/v Tween 80™, and 0.5% w/v Span 85™ and optionally contains various amounts of MTP-PE, formulated into submicron particles using a microfluidizer such as Model 110Y microfluidizer (Microfluidics, Newton, MA). For example, MTP-PE may be present in an amount of about 0-500 µg/dose, more preferably 0-250 µg/dose and most preferably, 0-100 µg/dose. As used herein, the term "MF59-0" refers to the above submicron oil-in-water emulsion lacking MTP-PE, while the term MF59-MTP denotes a formulation that contains MTP-PE. For instance, "MF59-100" contains 100 µg MTP-PE per dose, and so on. MF69, another submicron oil-in-water emulsion for use herein, contains 4.3% w/v squalene, 0.25% w/v Tween 80™, and 0.75% w/v Span 85™ and optionally MTP-PE. Yet another submicron oil-in-water emulsion is MF75, also known as SAF, containing 10% squalene, 0.4% Tween 80™, 5% pluronic-blocked polymer L121, and thr-MDP, also microfluidized into a submicron emulsion. MF75-MTP denotes an MF75 formulation that includes MTP, such as from 100-400 µg MTP-PE per dose.

Submicron oil-in-water emulsions, methods of making the same and immunostimulating agents, such as muramyl peptides, for use in the compositions, are described in detail in International Publication No. WO 90114837 and U.S. Patent Nos. 6,299,884 and 6,45 1,325, incorporated herein by reference in their entireties.

Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used as adjuvants in the invention.

C. Saponin Formulations

Saponin formulations, may also be used as adjuvants in the invention. Saponins are a heterologous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponin from the bark of the *Quillaia saponaria* Molina tree have been widely studied as adjuvants. Saponin can also be commercially obtained from *Smilax ornata* (sarsapilla), *Gypsophilla paniculata* (brides veil), and *Saponaria officianalis* (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs.

Saponin compositions have been purified using High Performance Thin Layer Chromatography (HP-LC) and Reversed Phase High Performance Liquid Chromatography (RP-HPLC). Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of

QS21 is disclosed in U.S. Patent No. 5,057,540. Saponin formulations may also comprise a sterol, such as cholesterol (see WO 96/33739).

Combinations of saponins and cholesterol can be used to form unique particles called Immunostimulating Complexes (ISCOMs). ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylcholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of Quil A, QHA and QHC. ISCOMs are further described in EP 0 109 942, WO 96/11711 and WO 96/33739. Optionally, the ISCOMS may be devoid of additional detergent. See ref. 11.

A review of the development of saponin based adjuvants can be found at ref. 12.

C. Virosomes and Virus Like Particles (VLPs)

Virosomes and Virus Like Particles (VLPs) can also be used as adjuvants in the invention. These structures generally contain one or more proteins from a virus optionally combined or formulated with a phospholipid. They are generally non-pathogenic, non-replicating and generally do not contain any of the native viral genome. The viral proteins may be recombinantly produced or isolated from whole viruses. These viral proteins suitable for use in virosomes or VLPs include proteins derived from influenza virus (such as HA or NA), Hepatitis B virus (such as core or capsid proteins), Hepatitis E virus, measles virus, Sindbis virus, Rotavirus, Foot-and-Mouth Disease virus, Retrovirus, Norwalk virus, human Papilloma virus, HIV, RNA-phages, Q β -phage (such as coat proteins), GA-phage, ϕ -phage, AP205 phage, and Ty (such as retrotransposon Ty protein p1). VLPs are discussed further in WO 03/024480, WO 03/024481, and Refs. 13, 14, 15 and 16. Virosomes are discussed further in, for example, Ref. 17

D. Bacterial or Microbial Derivatives

Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as:

(1) *Non-toxic derivatives of enterobacterial lipopolysaccharide (LPS)*

Such derivatives include Monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 De-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acylated monophosphoryl lipid A is disclosed in EP 0 689 454. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22 micron membrane (see EP 0 689 454). Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives e.g. RC-529. See Ref. 18.

(2) *Lipid A Derivatives*

Lipid A derivatives include derivatives of lipid A from *Escherichia coli* such as OM-174. OM-174 is described for example in Ref. 19 and 20.

(3) *Immunostimulatory oligonucleotides*

Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a sequence containing an unmethylated cytosine followed by guanosine and linked by a phosphate bond). Bacterial double stranded RNA or oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

The CpG's can include nucleotide modifications/analogs such as phosphorothioate modifications and can be double-stranded or single-stranded. Optionally, the guanosine may be replaced with an analog such as 2'-deoxy-7-deazaguanosine. See ref. 21, WO 02/26757 and WO 99/62923 for examples of possible analog substitutions. The adjuvant effect of CpG oligonucleotides is further discussed in Refs. 22, 23, WO 98/40100, U.S. Patent No. 6,207,646, U.S. Patent No. 6,239,116, and U.S. Patent No. 6,429,199.

The CpG sequence may be directed to TLR9, such as the motif GTTCGTT or TTCGTT. See ref. 24. The CpG sequence may be specific for inducing a Th1 immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such as a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in refs. 25, 26 and WO 01/95935. Preferably, the CpG is a CpG-A ODN.

Preferably, the CpG oligonucleotide is constructed so that the 5' end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3' ends to form "immunomers". See, for example, refs. 27, 28, 29 and WO 03/035836.

(4) *ADP-ribosylating toxins and detoxified derivatives thereof.*

Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the invention. Preferably, the protein is derived from *E. coli* (i.e., *E. coli* heat labile enterotoxin "LT", cholera ("CT"), or pertussis ("PT")). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is described in WO 95/17211 and as parenteral adjuvants in WO 98/42375. Preferably, the adjuvant is a detoxified LT mutant such as LT-K63.

E. Human Immunomodulators

Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as interleukins (e.g. IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12, etc.), interferons (e.g. interferon- γ), macrophage colony stimulating factor, and tumor necrosis factor.

F. Bioadhesives and Mucoadhesives

Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable bioadhesives include esterified hyaluronic acid microspheres (Ref. 30) or mucoadhesives such as cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrrolidone,

polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention. E.g., ref. 31.

G. Microparticles

Microparticles may also be used as adjuvants in the invention. Microparticles (*i.e.* a particle of ~100nm to ~150µm in diameter, more preferably ~200nm to ~30µm in diameter, and most preferably ~500nm to ~10µm in diameter) formed from materials that are biodegradable and non-toxic (*e.g.* a poly(α -hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, *etc.*), with poly(lactide-co-glycolide) are preferred, optionally treated to have a negatively-charged surface (*e.g.* with SDS) or a positively-charged surface (*e.g.* with a cationic detergent, such as CTAB).

H. Liposomes

Examples of liposome formulations suitable for use as adjuvants are described in U.S. Patent No. 6,090,406, U.S. Patent No. 5,916,588, and EP 0 626 169.

I. Polyoxyethylene ether and Polyoxyethylene Ester Formulations

Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters. Ref. 32. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol (Ref. 33) as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol (Ref. 34).

Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

J. Polyphosphazene (PCPP)

PCPP formulations are described, for example, in Ref. 35 and 36.

K. Muramyl peptides

Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

L. Imidazoquinolone Compounds.

Examples of imidazoquinolone compounds suitable for use as adjuvants in the invention include Imiquamod and its homologues, described further in Ref. 37 and 38.

The invention may also comprise combinations of aspects of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention:

- (1) a saponin and an oil-in-water emulsion (ref. 39);
- 5 (2) a saponin (e.g., QS21) + a non-toxic LPS derivative (e.g., 3dMPL) (see WO 94/00153);
- (3) a saponin (e.g., QS21) + a non-toxic LPS derivative (e.g., 3dMPL) + a cholesterol;
- (4) a saponin (e.g. QS21) + 3dMPL + IL-12 (optionally + a sterol) (Ref. 40);
- (5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions (Ref. 41);
- (6) SAF, containing 10% Squalane, 0.4% Tween 80, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion.
- (7) Ribi™ adjuvant system (RAS), (Ribi Immunochem) containing 2% Squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphoryl lipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (Detox™); and
- 15 (8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dPML).
- 20 Aluminium salts and MF59 are preferred adjuvants for parenteral immunisation. Mutant bacterial toxins are preferred mucosal adjuvants.

The composition may include an antibiotic.

Further antigens

The compositions of the invention may further comprise one or more additional non-GBS antigens, including additional bacterial, viral or parasitic antigens.

In another embodiment, the GBS antigen combinations of the invention are combined with one or more additional, non-GBS antigens suitable for use in a vaccine designed to protect elderly or immunocompromised individuals. For example, the GBS antigen combinations may be combined with an antigen derived from the group consisting of *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermis*, *Pseudomonas aeruginosa*, *Legionella pneumophila*, *Listeria monocytogenes*, *Neisseria meningitidis*, influenza, and Parainfluenza virus ('PIV').

Where a saccharide or carbohydrate antigen is used, it is preferably conjugated to a carrier protein in order to enhance immunogenicity {e.g. refs. 42 to 51}. Preferred carrier proteins are bacterial toxins or toxoids, such as diphtheria or tetanus toxoids. The CRM₁₉₇ diphtheria toxoid is particularly preferred {52}. Other carrier polypeptides include the *N.meningitidis* outer membrane

protein {53}, synthetic peptides {54, 55}, heat shock proteins {56, 57}, pertussis proteins {58, 59}, protein D from *H.influenzae* {60}, cytokines {61}, lymphokines, hormones, growth factors, toxin A or B from *C.difficile* {62}, iron-uptake proteins {63}, *etc.* Where a mixture comprises capsular saccharides from both serogroups A and C, it may be preferred that the ratio (w/w) of MenA
 5 saccharide:MenC saccharide is greater than 1 (*e.g.* 2:1, 3:1, 4:1, 5:1, 10:1 or higher). Different saccharides can be conjugated to the same or different type of carrier protein. Any suitable conjugation reaction can be used, with any suitable linker where necessary.

Toxic protein antigens may be detoxified where necessary *e.g.* detoxification of pertussis toxin by chemical and/or genetic means.

10 Where a diphtheria antigen is included in the composition it is preferred also to include tetanus antigen and pertussis antigens. Similarly, where a tetanus antigen is included it is preferred also to include diphtheria and pertussis antigens. Similarly, where a pertussis antigen is included it is preferred also to include diphtheria and tetanus antigens.

15 Antigens in the composition will typically be present at a concentration of at least 1 µg/ml each. In general, the concentration of any given antigen will be sufficient to elicit an immune response against that antigen.

As an alternative to using protein antigens in the composition of the invention, nucleic acid encoding the antigen may be used (*e.g.* refs. 64 to 72). Protein components of the compositions of the invention may thus be replaced by nucleic acid (preferably DNA *e.g.* in the form of a plasmid)
 20 that encodes the protein.

Definitions

The term "comprising" means "including" as well as "consisting" *e.g.* a composition "comprising" X may consist exclusively of X or may include something additional *e.g.* X + Y.

25 The term "about" in relation to a numerical value x means, for example, $x \pm 10\%$.

References to a percentage sequence identity between two amino acid sequences means that, when aligned, that percentage of amino acids are the same in comparing the two sequences. This alignment and the percent homology or sequence identity can be determined using software programs known in the art, for example those described in section 7.7.18 of reference 73. A preferred
 30 alignment is determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is disclosed in reference 74.

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WHAT IS CLAIMED IS:

1. A composition comprising a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof or a polypeptide sequence having 50% or greater sequence identity thereto.
2. The composition of claim 1, wherein said combination of GBS antigens demonstrates improved immunogenicity as measured by the Active Maternal Immunization Assay, wherein said Active Maternal Immunization Assay measures serum titers of female mice during an immunization schedule and percent survival rate of pups after challenge.
3. The composition of claim 2, wherein the percent survival rate of challenged pups is at least 2 percentage points higher than the percent survival rate of challenged pups from female mice immunized with a single non-GBS 80 antigen.
4. The composition of claim 1, wherein said combination consists of two GBS antigens.
5. The composition of claim 1, wherein said combination consists of three GBS antigens.
6. The composition of claim 1, wherein said combination consists of four GBS antigens.
7. The composition of claim 1, wherein said combination consists of five GBS antigens.
8. The composition of claim 1, wherein GBS 80 comprises the amino acid sequence of SEQ ID NO 2 or an immunogenic fragment thereof.
9. The composition of claim 1, wherein the fragment of GBS 80 comprises the amino acid sequence selected from the group consisting of SEQ ID NOS: 3, 4, 5, 6, 7, 8, and 9.
10. The composition of claim 1, said combination consisting of two to thirteen GBS antigens selected from the group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.
11. The composition of claim 1, said combination including GBS 80, GBS 104 and GBS 322.
12. The composition of claim 1, said combination including GBS 80, GBS 104, GBS 276 and GBS 322.
13. The combination of claim 1 wherein said combination comprises at least one of GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, or GBS 691.

14. A fusion protein comprising a portion of a GBS 80 antigen and a portion of at least one GBS antigen.
15. The fusion protein of claim 14 wherein said at least one GBS antigen is selected from the group consisting of GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, or GBS 691.
16. The fusion protein of claim 15 wherein said at least one GBS antigen is GBS 322.
17. The fusion protein of claim 16 consisting essentially of a GBS 80 antigen and a GBS 322 antigen.
18. A method for the therapeutic or prophylactic treatment of GBS infection in an animal susceptible to GBS infection comprising administering to said animal a therapeutic or prophylactic amount of the composition of claim 1.
19. A method for the manufacture of a medicament for raising an immune response against GBS comprising combining a GBS 80 antigen or fragment thereof with at least one GBS polypeptide antigen.
20. The method of claim 19 wherein said at least one GBS polypeptide antigen comprises a polypeptide or fragment thereof selected from the antigen group consisting of GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.
21. Use of the compositions of any one of claims 1-17 in the preparation of a medicament for treatment of GBS infection.

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60/548,789 26 February 2004 (26.02.2004) US(71) Applicant (for all designated States except US): **CHIRON CORPORATION** [US/US]; 4560 Horton Street, Emeryville, CA 94608-2916 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **RAPPUOLI, Rino** [—/US]; c/o Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097 (US).(74) Agent: **HALE, Rebecca, M.**; Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608-2916 (US).

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Published:

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMMUNOGENIC COMPOSITIONS FOR *STREPTOCOCCUS AGALACTIAE*

(57) Abstract: This application relates to Group B Streptococcus ("GBS") vaccines comprising combinations of GBS polypeptide antigens where the polypeptides contribute to the immunological response in a recipient. Preferably, the compositions of the invention comprise a combination of two or more GBS antigens, wherein said combination includes GBS 80 or a fragment thereof. In one embodiment, the combination may consist of two to thirteen GBS antigens selected from an antigen group consisting of GBS 80, GBS 91, GBS 104, GBS 184, GBS 276, GBS 305, GBS 322, GBS 330, GBS 338, GBS 361, GBS 404, GBS 690, and GBS 691.

WO 2005/028618 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/30032

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 39/385, 39/116, 39/00, 39/02, 39/38, 39/09
 US CL : 424/197.11, 203.1, 192.1, 190.1, 184.1, 244.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/197.11, 203.1, 192.1, 190.1, 184.1, 244.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/041157 A2 (CHIRON CORPORATION) 21 May 2004 (21.05.2004), claims, and pages 4 and 5.	1-17

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

Ister document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, each combination being obvious to a person skilled in the art

"Z"

document member of the same patent family

Date of the actual completion of the international search

09 November 2005 (09.11.2005)

Date of mailing of the international search report

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 Commissioner for Patents
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 Alexandria, Virginia 22313-1450
 Facsimile No. (571) 273-3201

Authorized officer

S. Devi, Ph.D.

Telephone No. (571) 272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/30032

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-17

- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/30032

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-17, drawn to a composition comprising a combination of two or more GBS antigens comprising GBS 80 or a fragment thereof.

Group II, claim(s) 18, drawn to a method for the therapeutic or prophylactic treatment of GBS infection by administering the composition of invention I.

Group III, claim(s) 19-21, drawn to a method for the manufacture of a medicament by combining a GBS 80 antigen fragment thereof with at least one GBS polypeptide antigen.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Inventions I-III lack unity. The special technical feature of invention I is a composition comprising a combination of two or more GBS antigens comprising GBS 80 or a fragment thereof. However, such a composition was already disclosed in the prior art. For instance, CHIRON CORPORATION (WO 2004/041157 A2) disclosed a composition comprising a combination of GBS 80 having the amino acid sequence of SEQ ID NO: 2 and GBS 322 antigen. Thus, the product of invention I does not define over the prior art. Although the product of invention I and the method of using the product of invention II and a method of making the product of invention III is a permitted combination under PCT Rule 13.2, in the instant case, since the product of invention I is already disclosed in the art, the special technical feature is not a unifying feature. Technically, the absence of special technical feature permits the separation of the method of using the product or the method of making the product from the product itself.

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/30032

DIALOG, WEST, MEDLINE, BIOSIS, EMBASE, Sequence databases
GBS 80, SEQ ID NO: 2, inventors' names